MANAGEMENT OF PAIN DURING INTRAUTERINE DEVICE INSERTION

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A

PROJECT

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Abstract

Increased use of intrauterine contraception is desirable to achieve safe, highly effective, long-acting, and reversible means to prevent unintended pregnancy. For most women, intrauterine device (IUD) contraception is a viable option for protection from an unplanned pregnancy. Fear of pain during insertion is one barrier to IUD use. The aim of this project was to identify best practice evidence for different types of interventions for the management of pain during IUD insertion. Evidence for pain management strategies was critically appraised, and the most recent information synthesized into evidence-based recommendations to promote point-of-care decisions.

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Background

Forty three million women in their childbearing years in the United States (U.S.) are at risk of unintended pregnancy (Guttmacher Institute, 2015). Long-acting reversible contraceptive methods, including intrauterine devices (IUD), are safe and highly effective contraceptive methods (Centers for Disease Control and Prevention [CDC], 2013). Failure rates for IUDs are less than one percent, and they can be used by women of all ages including adolescents and nulliparous women (CDC, 2013). Usage rates of long-acting reversible contraceptives in the U.S. increased from 2.4 % in 2002 to 8.5 % in 2009 with most women relying on IUDs (Finer, Jerman, & Kavanaugh, 2012). Increased use of IUDs is desirable to achieve safe, highly effective, long-acting and reversible means to prevent unintended pregnancy (Allen, Carey, Raker, & Matteson, 2014).

Fear of pain during insertion of an IUD may deter women from choosing the IUD as a method of contraception (Finer et al., 2012). Pain during insertion of an IUD can be associated with multiple causes including applying the tenaculum to the cervix to straighten the cervical canal, passing the uterine sound, inserting the IUD through the cervix, and myometrial contractions caused by the IUD irritating the uterine cavity (Allen, Bartz, Grimes, Hubacher, & O'Brien, 2009). Pharmacological interventions for pain control during IUD insertion include analgesics, local anesthetics, and the use of prostaglandins to soften the cervix; however, there is wide variation in the use of these methods (Allen et al., 2009). Other non-pharmacological considerations such as pre-insertion counseling, the setting for the procedure, or the confidence of the provider may influence a women's level of anxiety, possibly affecting her perception of pain and the overall experience (Gemzell-Danielsson, Mansour, Fiala, Kaunitz, & Bahamondes, 2013).

Offering and providing pain relief during IUD insertion is usually at the discretion of the provider or site where the service is being provided (Akintomide et al., 2013). Also, healthcare providers often underestimate patients' pain during IUD insertion (Maguire, Morrell, Westhoff, & Davis, 2013), and differ in their opinions on women's perceptions of pain or discomfort (Akintomide et al., 2013). An understanding of the relationship between provider and patient perceptions of pain, as well as knowledge of techniques to ease IUD insertion-related pain can promote patient comfort and satisfaction with care. Determining an optimal method for reducing pain during IUD insertion benefits both women and healthcare providers.

Literature Review

Management of pain during IUD insertion has the potential to improve usage rates for women seeking long-acting reversible contraception. Factors affecting greater pain associated with IUD insertion will be discussed. All articles selected for this review incorporate both pharmacological and non-pharmacological interventions for managing pain during IUD insertion. Finally, limitations in the available literature will be addressed to highlight the need for this project.

Pain during IUD Insertion

Review of the literature identified that pain during IUD insertion is multifactoral and difficult to predict. According to Hubacher et al. (2006) predictors of increased pain during IUD insertion include nulliparity, age greater than 30 years, lengthier time since last pregnancy or last menses, and not currently breastfeeding. Allen et al. (2014) predicted pain to be greater based on history of no previous vaginal delivery, and difficulty of the procedure. The authors also identified higher expected pain and lower self-reported pain tolerance to be variables predictive of increased pain.

The level of pain women experienced during IUD insertion varied in published studies. Mild to moderate pain is expected during IUD insertion, but for some women the pain is substantial (Gemzell-Danielsson et al., 2013). A prospective study revealed 78% of nulliparous women rated IUD insertion pain as moderate to severe (Hall & Kutler, 2015). Also, a proportion of parous women (11%) reported severe pain (Heikinheimo et al., 2010). Strategies for effective pain management during IUD insertion are needed for these women.

Pharmacological Interventions for Pain

There are multiple reviews and opinions in the literature regarding available pharmacological interventions for managing pain during IUD insertion. These include analgesia, local anesthesia, and cervical priming. Nonsteroidal anti-inflammatory drugs (NSAIDs) may reduce cervical or uterine pain because they act to block the cyclooxygenase enzyme from producing prostaglandin, thereby inhibiting inflammation (Edmunds & Mayhew, 2014). The analgesic action of nitrous oxide is thought to be from stimulation of endogenous endorphins, and possibly corticotrophins and dopamine, creating euphoria that makes the patient less aware of pain (Rosen, 2002). Local anesthesia decreases pain by blocking nerve conduction and causing a loss of sensation (Edmunds & Mayhew, 2014). Prior to insertion of an IUD, the use of a prostaglandin such as misoprostol causes dissolution of collagen fibers in the cervix and may decrease pain by dilating and softening the cervix (Allen et al., 2009).

The use of analgesia with NSAIDs for IUD insertion-related pain is widespread (Gemzell-Danielsson et al., 2013), despite the lack of supporting evidence of their efficacy (Carusi & Goldberg, 2015). Nitrous oxide has been used for years for procedural analgesia in outpatient settings and has recently been investigated as an approach to pain management in the context of IUD insertion (Singh et al., 2015). Local anesthesia was found to be used more by

providers working in integrated reproductive health and contraceptive-only services compared to those in general practice (Akintomide et al., 2013). An online U.S. based survey reported 40% of providers routinely used misoprostol for cervical ripening in nulliparous women, but there were wide variations in timing, dose, and route of administration (Gemzell-Danielsson et al., 2013). According to Pergialiotis, Vlachos, Protopappas, & Vlachos (2014), pain intervention options for placement of IUDs are conflicting and inconclusive.

Non-pharmacological Interventions for Pain

The literature also revealed non-pharmacological interventions for pain relief with IUD insertion including delayed bladder emptying, aromatheraphy, pre-placement counseling, and distraction during the procedure. Cameron, Glassier, Cooper, & Johnstone (2013) investigated delayed versus immediate bladder emptying for IUD insertion, but found no significant difference in reported pain scores. Use of aromatherapy as complementary treatment has been examined and shown to reduce anxiety associated with IUD insertion (Shahnazi, Nikjoo, Yavarikia, & Mohammad-Alizadeh-Charandabi, 2012). Pre-placement counseling and distraction were also found to be effective at reducing anxiety (Bahamondes, Mansour, Fiala, Kaunitz, & Gemzell-Danielsson, 2014). Further evaluation of additional interventions in managing IUD insertion-related pain is warranted.

Limitations

No guidelines are available that detail standardized approaches to the problem of managing IUD insertion-related pain for those women requiring, or requesting a pain relief intervention (Bahamondes et al., 2014). A Cochrane review (2009) which included trials from 1974 to 2007 highlighted the need for an updated evaluation of interventions for pain with IUD. *UpToDate*, a premier web-based, evidence-based decision support resource provided limited data

on additional interventions for relieving IUD insertion pain (Carusi & Goldberg, 2015). Patient anxiety about the procedure may contribute to higher levels of perceived pain, suggesting further exploration of interventions to decrease anxiety during the procedure is needed; however, no studies of the role of non-pharmacological reduction of anxiety have been published (Bahamondes et al., 2014).

Purpose

Fear of pain has an impact on women choosing an IUD for birth control. Management of pain during IUD insertion has the potential to improve the outcome for women desiring long-acting reversible methods of contraception. A critical appraisal of the literature was conducted with the objective of identifying interventions for managing pain associated with the insertion of IUDs. Evidence of pain management strategies was evaluated and the most recent information available since 2010 synthesized into evidence-based recommendations. The aim of this project was to critically evaluate the evidence for various pain management strategies and formulate evidence-based recommendations to promote point-of-care decision-making (see Appendix A).

Evidence Based Practice Model: The Star Model of Knowledge Transformation

The Star Model of Knowledge Transformation (Figure 1) was utilized for this project as it provided an organizing framework for systematically identifying and transforming the evidence into recommendations for practice. This model uses five star points to organize the complexity and volume of available knowledge, and depicts five stages of knowledge transformation. These stages of knowledge transformation include a) discovery research, b) evidence summary, c) translation to guideline, d) practice integration, and e) process outcome evaluation (Stevens, 2012).

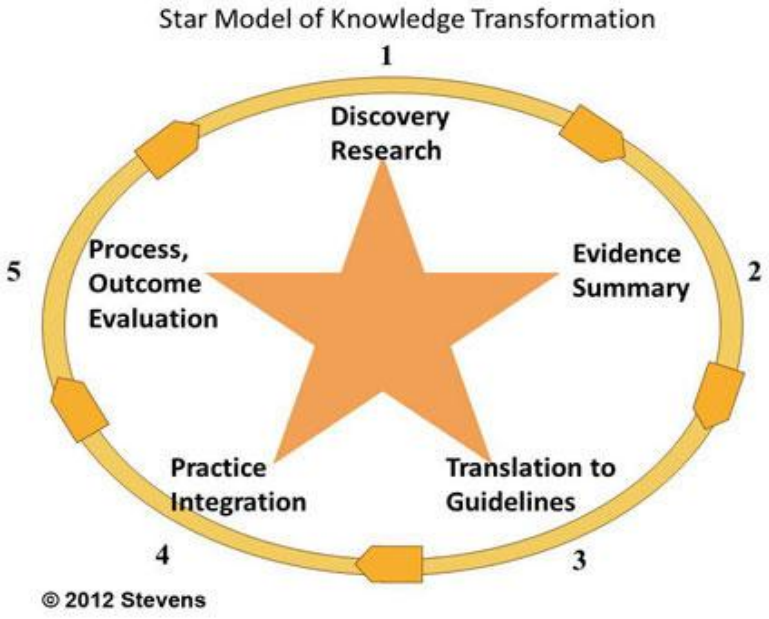

Figure 1. Star Model of Knowledge Transformation. "Copyrighted material (Stevens, 2012). Reproduced with expressed permission" (see Appendix B).

Discovery represented the knowledge inquiry stage regarding available interventions for managing pain during IUD insertion. The evidence summary stage combined all the findings from the research studies, and reduced the large amount of literature into a manageable form. In this project, a critical appraisal of all studies that could answer the research question was done in order to identify strategies for the management of IUD insertion-related pain. The evidence was translated to produce valid and reliable clinical recommendations to enhance the management of pain during IUD insertion. Practice integration is crucial to verify the success of this project in establishing best-evidence recommendations for use by primary care providers in clinical practice; however, it is important to include not only the healthcare provider but also the patient and system outcomes in the final evaluation phase (Melnyk & Fineout-Overholt, 2010). This portion of the model was outside the scope of this project; however, a future project is suggested to assess the usefulness and applicability of the recommendations.

Methods

Rights of Human Subjects

As this project is an analysis of metadata available through published sources, there was no requirement for human protection review. An Institutional Review Board (IRB) application was submitted per graduate school requirements, and exempt status was assigned. A copy of exempt IRB approval is included in the manuscript (see Appendix C).

Project Design

A critical appraisal of the literature was conducted to identify evidence-based best practice for the management of pain for women having an IUD placed. "An intellectual critical appraisal of a study involves a careful and complete examination of a study to judge its strengths, weaknesses, meaning, credibility, and significance for practice" (Grove, Gray, & Burns, 2015, p. 365). Guidelines for the critical appraisal included: examination of the expertise of the authors, reviewing the entire study, addressing the strengths and weaknesses of each study, and evaluating study findings to determine implications for practice. A critical appraisal table was utilized to summarize and evaluate the findings from the appraisal (see Appendix D). The evidence was ranked according to the John Hopkins nursing evidence based practice system for hierarchy of evidence table (see Appendix E).

Search Strategy

The goal of the search strategy was to identify studies published in the last five years. The databases utilized for the review included *PubMed, CINAHL, Cochrane Database of Systematic Reviews, the Cochrane Central Register of Controlled Trials,* and *ClinicalTrials.gov.* The search for unpublished studies also included *Google Scholar,* and *ProQuest Dissertation and Theses Global*. Database searches included the keywords 'intrauterine device', 'insertion',

and 'pain'. The search was then further refined by combining context search terms "OR" and "AND." Reference lists were also checked for additional studies to ensure all relevant articles had been identified. Studies in languages other than English were excluded as resources for translation were limited.

Data Collection

Research studies selected for critical appraisal were based on the timeline of published work, population, condition of interest, interventions of interest, and comparison interventions of interest. Articles published from 2010 to the present were selected for critical appraisal and evaluated based on their significance to the project topic of best practice pain interventions for IUD insertion. The critical appraisal evaluated studies that included the outcome measure: perceived pain during IUD insertion. The population focus for this project was women having any type of IUD inserted. The interventions and comparison interventions of interest included studies that evaluated any type of pain reduction strategy, including pharmacologic or other intervention administered prior to or during IUD insertion.

Data Synthesis

Each grid of the critical appraisal table contains the following information: American Psychological Association (APA) citation, study method, population, variables, measurement, data analysis, findings, and level of evidence. This allowed for comparative analysis of study design; number and characteristics of patients; type of intervention; scale used to measure outcome variable; statistics used to answer the clinical question and significance of pain reduction effect; statistical findings; and worth or feasibility of use in advanced nursing practice. To assess evidence quality and address confidence in the recommendations from this project, the John Hopkins nursing evidence based practice hierarchy of evidence was utilized to determine

the overall strength of each article included in the critical appraisal. According to this hierarchy, systematic reviews of randomized control trials, experimental/ randomized controlled trials (RCT) or meta-analysis of RCTs are assigned a level I. Level I is considered the strongest level and represents high-quality evidence.

Results

The initial search utilizing *EBSCOhost* resulted in 82 articles. The title and abstract of each article was reviewed to determine if inclusion criteria were met, and duplicates were removed. Of these, 26 studies were catalogued into the critical appraisal table (see Appendix F). Each article was fully read and individually reviewed paying careful attention to study design, validity of findings, and usefulness of the results. An additional three relevant articles were identified from reference lists of articles reviewed. Ultimately, a total of 29 studies were deemed appropriate for inclusion, all of which were of level I evidence.

Discussion

Evidence Summary

The pharmacological interventions identified included the use of analgesia, local anesthesia, and cervical priming. Strategies for non-pharmacological pain management included delayed bladder emptying, aromatherapy, psychological preparation/counseling before insertion and distraction during the procedure. The evidence for each of these strategies and implications for practice are presented.

Analgesia. Five RCTs have evaluated the use of analgesia for the management of pain associated with IUD insertion (Table 1). Analgesics included the NSAIDs ibuprofen, naproxen sodium and ketorolac, the atypical opioid tramadol, and inhaled nitrous oxide. NSAIDs such as naproxen and ibuprofen reduce pain by blocking cyclooxygenase enzyme activity and the

formation of exogenous prostaglandin (Bednarek et al., 2015; Chor, Bregand-White, Golobof, Harwood, & Cowett, 2012). Ketorolac is a potent NSAID indicated for short-term moderate acute pain with a quicker onset of action compared with oral medications (Ngo, Ward, & Mody, 2015). Tramadol is an atypical opioid that inhibits reuptake of serotonin and norepinephrine, as well as exhibiting weak μ-agonist activity and is widely used to treat moderate to severe pain (Karabayirli, Ayrim, & Muslu, 2012). Nitrous oxide has analgesic and anxiolytic properties thought to be from stimulation of endogenous endorphins, and possibly corticotrophins and dopamine, creating euphoria that makes the patient less aware of pain (Rosen, 2002).

Table 1

Studies Evaluating Analgesia Used for Pain during IUD Insertion

Reference	**n**	**Population**	**Intervention**	**Significance of pain reduction effect**	**Level of evidence**
Bednarek et al (2015)	202	Nulliparous and parous	800 mg ibuprofen or placebo orally	Not significant (mean scores 38 vs 41.5, $p = 0.5$)	1
Ngo et al (2015)	67	Nulliparous and parous	30 mg ketorolac or normal saline placebo intramuscularly	Not significant (median pain scores 3.6 vs 5.2, $p = 0.99$)	1
Singh et al (2015)	80	Nulliparous	50/50 nitrous oxide/oxygen or oxygen inhaled	Not significant (mean scores 54 vs 55; $p = 0.85$)	I
Chor et al (2012)	81	Mainly parous	800 mg ibuprofen or placebo orally	Not significant (mean scores 3.9 vs 3.3, $p = 0.91$)	1
Karabayirli et al (2012)	103	Parous	50 mg tramadol or 550 mg naproxen sodium or placebo orally	Significant reduction in mean pain scores with tramadol vs naproxen sodium (2.31 vs 2.94, $p = 0.003$) and with naproxen vs placebo (2.9 vs 4.8, $p = 0.001$)	I

Ibuprofen. In the first RCT, 202 women received either 800 mg ibuprofen or placebo 30 to 40 minutes prior to IUD insertion (Bednarek et al., 2015). Ibuprofen had no significant effect on patient-reported pain compared with placebo. Parity was a significant predictor of pain. The subgroup of nulliparous women experienced approximately twice as much pain compared with multiparous women, but ibuprofen had no clinically relevant impact on the level of pain compared with placebo.

The second RCT randomized 81 women to receive either 800 mg ibuprofen or placebo 45 minutes before insertion of an IUD (Chor et al., 2012). Consistent with the above trial that failed to find a difference in pain at the time of IUD insertion between women receiving ibuprofen or placebo, prophylactic use of ibuprofen had no significant impact on mean scores of pain. Mean pain scores in both the placebo and ibuprofen study groups indicated a need for managing pain during the insertion procedure.

Ketorolac. The third RCT evaluated pain control of intramuscular ketorolac 30 mg compared with placebo saline solution injection prior to IUD insertion in 67 women (Ngo et al., 2015). Although there was not a clinically significant difference between pain scores in the placebo compared to the ketorolac group during IUD insertion, there was a decrease in pain scores at five and fifteen minutes. The maximal effect of ketorolac is at one to two hours; however, the study was done at 30 minutes. The majority of participants felt pain from the injection was “not as bad” as pain from IUD placement (71% compared with 81%); however, 20% reported injection site pain was "as bad" as IUD placement. Median pain scores were higher in the nulliparous subgroup compared with multiparous subgroup.

Nitrous oxide. One RCT evaluated a fixed blend of 50% nitrous oxide with 50% oxygen versus 100% oxygen as placebo inhaled through a mask during IUD insertion in 80 nulliparous

women (Singh et al., 2015). Although pain scores at the time of IUD insertion were slightly lower in the nitrous oxide group than in the oxygen group, the difference was not significant. However, significantly more women in the nitrous oxide group were more satisfied with their pain management, suggesting the usefulness of self-administered nitrous oxide for its anxiolytic proeprties. In the United Kingdom, Sewell and Vincent (2015) have been offering nitrous oxide for reducing the pain of IUD insertion and have had a positive response; the authors plan to publish results of the trial.

***Tramadol versus naproxen sodium*.** In the fifth RCT, 103 women received 50 mg of tramadol, 550 mg naproxen sodium, or placebo one hour before IUD insertion (Karabayirli et al., 2012). Tramadol demonstrated superior analgesia over naproxen and placebo with pain scores in the tramadol group significantly lower than in the naproxen group. Naproxen sodium was also associated with a significant reduction in pain compared with placebo. Although tramadol mean scores were significantly lower when compared with the naproxen group, this difference may not be clinically significant as the pain score in both groups were similar.

Anesthesia. The use of local anesthesia in the management of pain for IUD insertion has been evaluated in eleven studies (Table 2). The studies included the use of lidocaine in a number of formulations: gel, cream, spray, and injection; with differing techniques of administration: topical, intracervical and paracervical. Lidocaine has a rapid onset of around two minutes or less and duration of action of 30 to 60 minutes, but is liable to vary among application sites (Tornblom-Paulander et al., 2015). Allowing adequate time to elapse between the administration of lidocaine and IUD insertion is necessary for it to take effect (Tornblom-Paulander et al., 2015).

Table 2

Studies Evaluating Anesthetics for Managing Pain during IUD Insertion

Author	**n**	**Population**	**Interventions**	**Significance of pain reduction effect**	**Level of evidence**
Aksoy et al. (2015)	200	Parous	10% lidocaine or isotonic saline spray 3 mins prior	Significant (mean scores 1.01 vs. 3.23; $p < 0.001$)	I
Tavakolian et al. (2015)	92	Parous	Lidocaine-prilocaine EMLA or placebo cream 7 mins prior	Significant (mean scores 2.65 vs. 4.61; $p < 0.001$)	I
Tornblom-Paulander et al. (2015)	218	Parous and nulliparous	Lidocaine 4% or placebo gel 5 mins prior	Significant (28.3 vs. 44.2; $p < 0.001$)	I
Castro et al. (2014)	100	Nulliparous	2% lidocaine injected 5 minutes prior or 400 mg or ibuprofen orally one hr prior	Not significant (effect size < 10%) but showed risk of moderate/severe pain reduced by 40%	I
Allen, Raker, & Goyal (2013)	145	Parous and nulliparous	2% lidocaine or placebo gel 3 mins prior	Not significant (mean scores 35.2 vs. 36.7; $p = .8$)	I
Cirik et al. (2013)	95	Mostly parous	1% lidocaine or 0.9% NaCl paracervical block or no analgesia	Significant (median pain 2 vs. 6. vs 6; $p < .001$)	I
Nelson & Fong (2013)	40	Parous and nulliparous	2% lidocaine or normal saline infused into endometrial cavity 3 minutes prior	Not significant (mean scores 3.0 vs. 3.7; $p = .40$)	I
Maguire et al. (2012)	200	Parous and nulliparous	2% lidocaine or placebo gel for 1 min	Not significant (mean scores 50.9 vs. 51.0; $p = .98$)	I
McNicholas et al. (2012)	199	Parous and nulliparous	2% lidocaine or placebo gel	Not significant (median pain score 5 vs. 6; $p = .20$)	I
Mody et al. (2012)	50	Parous and nulliparous	1% lidocaine paracervical or no anesthesia	Not significant (median score 24.0 vs. 62.0; $p = .09$)	I
Mohammad-Alizadeh-Charandabi et al. (2012)	96		2% lidocaine or placebo gel or no intervention 1 min prior	Not significant (mean scores 3.4 vs. 3.4 vs. 3.7)	I

Lidocaine topical gel. The application of lidocaine topical gel before IUD insertion has been evaluated in five RCTs. Four trials compared 2% lidocaine gel versus placebo; one trial included a group with no intervention. Allen et al. (2013) applied gel at the anterior lip of the cervix and into the cervical canal. McNicholas et al. (2012) applied gel to the ectocervix as well as via angiocatheter into the endocervical canal three minutes prior to application of the tenaculum. Tornbloom-Paulander (2015) applied gel on the surface of the cervix, into the cervical canal, and also into the uterine cavity and for five minutes prior to IUD insertion. Maguire et al. (2012) applied 2% lidocaine gel or placebo gel soaked onto a cotton swab and inserted into the cervix for one minute. In the fourth trial 2% lidocaine gel was used intracervically and on the outer part of the cervix where the tenaculum is placed, and was compared to placebo as well with no intervention (Mohammad-Alizadeh-Charandabi et al., 2012).

Pain during IUD insertion did not differ significantly in all the trials. Lidocaine gel did not reduce pain, even among nulliparous women (Allen et al., 2013; Maguire et al., 2012); however, McNicholas et al. (2012) reported significantly different insertional pain scores between nulliparous and multiparous women regardless of the intervention. Despite the finding that nulliparous women had significantly higher pain scores, reported pain was not different for nulliparous women randomized to intracervical lidocaine (McNicholas et al., 2012). Lidocaine treatment was associated with a decrease in pain in patients with severe dysmenorrhea ($p = .04$) (Allen et al., 2013).

A fifth trial examined use of 8.5 mL of a short-acting 4% lidocaine gel on the cervix, in the cervical canal, and into the uterine cavity five minutes before IUD insertion; all participants were nulliparous (Tornblom-Paulander et al., 2015). Mean pain scores were significantly lower

in the lidocaine group versus the placebo group, representing a 36% reduction in maximum pain. The authors noted that a significantly higher percentage in the lidocaine group was essentially pain-free, and a significantly lower percentage had moderate to severe pain. This study was a double-blind, phase -II study with sufficient statistical power to demonstrate the efficacy of lidocaine versus placebo, and included as many as 15 providers across three centers, increasing the likelihood of results being representative for clinical practice.

Lidocaine/prilocaine topical cream. One study evaluated euteric mixture of local anesthetics (EMLA) cream, consisting of 2.5% lidocaine and 2.5% prilocaine in 92 women as analgesia for IUD insertion (Tavakolian, Doulabi, Baghban, Mortazavi, & Ghorbani, 2015). Investigators applied 5 grams to the cervix using a cotton swab seven minutes prior to IUD insertion. Participants in the EMLA group had significantly reduced pain during IUD insertion.

Lidocaine infusion or spray. Two trials compared a different application method by administering lidocaine versus normal saline as a spray or an infusion. In the first RCT investigators used four pumps of 10% lidocaine spray or placebo in 200 parous women three minutes before IUD insertion (Aksoy, Aksoy, Ozyurt, Acmaz, & Babayigit, 2015). A significantly lower score for overall pain during IUD insertion was found in the treatment group compared to controls, and no systemic effects were observed with the 10% lidocaine spray. In the second RCT, a pilot study (n = 40), Nelson and Fong (2013) infused 2% lidocaine or placebo using a Pipet Curet endometrial aspirator into the lower third, middle, and top of the uterine cavity. Mean pain scores did not differ significantly between the lidocaine and the normal saline group, even in the eleven women who took NSAIDs before insertion.

Lidocaine block. Three trials injected lidocaine compared to placebo, no intervention, or ibuprofen orally. Two studies compared paracervical block of 1% lidocaine to no intervention as

control (Cirik, Taskin, Tuglu, Ortac, & Dai, 2013; Mody et al., 2012) or to saline as placebo (Cirik et al., 2013). IUD insertion occurred three minutes before (Mody et al., 2012), or five minutes before IUD insertion (Cirik et al., 2013). Although Mody et al. (2012) found a statistically significant decrease in pain during tenaculum placement, median pain scores in the paracervical lidocaine group were lower but they were not statistically significant. In the second trial study, median pain scores were significantly lower in the lidocaine paracervical group compared with saline placebo and with no intervention during IUD insertion (Cirik et al., 2013). The third trial compared an intracervical block of 2% lidocaine five minutes before IUD insertion, versus 400 mg ibuprofen orally one hour prior to the procedure in 100 women who were nulliparous or without previous vaginal delivery (Castro et al., 2014). Pain did not differ between the two groups, although intracervical anesthesia reduced moderate to severe pain by 40% but without statistical significance.

Cervical priming. The impact of cervical priming on pain associated with IUD insertion has been evaluated in eight RCTs with misoprostol, a prostaglanding analog, and two pilot studies examined the nitric oxide donors, nitroglycerin and nitroprusside (Table 3). Cervical priming refers to dilating or softening of the cervix prior to IUD placement which may reduce pain during the insertion procedure. Misoprostol acts on the cellular matrix of the cervix causing dissolution of collagen fibers and increasing the amount of fluid in the stroma resulting in cervical effacement (Scavuzzi et al., 2013). Route for administration of misoprostol included oral (buccal and sublingual) and vaginal; however, time of administration prior to the IUD insertion procedure varied. Nitroprusside and nitroglycerine are smooth muscle relaxants with the potential to induce cervical ripening without causing uterine cramping, the most significant side effect of misoprostol (Micks et al., 2014).

Table 3

Published Studies about Cervical Priming to Facilitate IUD Insertion

Author	**n**	**Population**	**Interventions**	**Significance of pain reduction effect**	**Level of evidence**
Bednarek et al. (2015)	24	Nulliparous	10 mg nitroprusside or placebo gel (intracervical) immediately prior	Not significant (61 vs 74, $p = 0.18$)	Pilot study
Micks et al. (2014)	24	Mostly nulliparous	0.5 mg nitroglycerin or placebo gel (vaginal) 30 min prior	Not significant (57.4 vs 55, $p = 0.82$)	Pilot study
Esprey et al. (2014)	85	Nulliparous	400 mcg misoprostol or placebo (orally) 2 - 8h prior	Not significant (58 vs 59, $p = 0.94$)	1
Lathrop et al. (2013)	71	Nulliparous	400 mcg misoprostol or placebo (orally) 2 - 4 hours prior	Significant but for increased pain (46.5 vs 35.1, $p = 0.04$)	1
Scavuzzi et al. (2013)	179	Nulliparous	400 mcg misoprostol or placebo (vaginal) 4 hours prior	Significant (44% reduction misoprostol group, $p = 0.00004$)	1
Ibrahim & Ahmed (2013)	200	Parous	400 mcg misoprostol (sublingual) and 100 mg diclofenac (oral) vs diclofenac 1 hour prior	Not significant (70 vs 65, $p = 0.8$)	1
Swenson et al. (2012)	105	Nulliparous	400 mcg misoprostol or placebo (vaginal) 3-4 hours prior	Not significant (58.4 vs 56.9, p = 0.74)	1
Edelman et al. (2011)	35	Nulliparous	400 mcg misoprostol or placebo (orally) 90 min prior	Not significant (65 vs 55, $p = 0.83$)	1
Dijkhuizen et al. (2010)	270	Nulliparous and parous	400 mcg misoprostol or placebo (vaginal) 3hours prior	Not significant (46 vs 40, $p = 0.14$)	1
Heikinheimo et al. (2010)	89	Mostly parous	400 mcg misoprostol or placebo (sublingual) 3hours prior	Not significant (misoprostol group vs placebo did not report less pain)	1

Nitroprusside and Nitroglycerin. The first randomized, double-blinded, placebo-controlled pilot study compared 10 mg nitroprusside compounded into a 1% aqueous gel with an identical-appearing placebo gel intracervically in 24 nulliparous women immediately before IUD insertion (Bednarek et al., 2015). The second pilot study compared 0.5 mg nitroglycerin ointment and identical placebo ointment applied vaginally at the posterior fornix 30 to 45 minutes prior to IUD insertion in 24 nulliparous women (Micks et al., 2014). Subjects were given the option of taking ibuprofen prior to the procedure. In both pilot studies, there were no statistically significant differences between mean pain scores, ease of insertion, or reports of side effects in treatment groups.

Vaginal misoprostol. Three RCTs evaluated misoprostol inserted vaginally for cervical priming prior to IUD insertion. In the first trial, 400 mcg of misoprostol vaginally three hours before IUD insertion versus placebo was evaluated in 199 nulliparous and multiparous women (Dijkhuizen et al., 2010). No difference in pain scores between the groups was found; however, there was a non-significant trend towards increased pain in the misoprostol group, and among the subgroup of nulliparous women pain scores and healthcare provider difficulty of insertion were higher. There was a statistically significant increase in side effects experienced by the misoprostol group compared with the placebo group, most commonly abdominal cramping.

Misoprostol 400 mcg inserted vaginally was also compared to placebo in the second trial, but it was placed four hours prior to the procedure (n = 179), and only included nulliparous women (Scavuzzi, Souza, Costa, & Amorim, 2013). In this study, the misoprostol group had a significant 44% reduction in moderate-to-severe pain compared with the placebo group. Although less subjective healthcare provider difficulty in inserting the IUD was reported, there was a greater incidence of cramps.

The third trial randomized participants to self-administer either 400 mcg of misoprostol or placebo, and they were instructed to insert it vaginally or orally three to four hours before the IUD appointment (Swenson et al., 2012). Data was analyzed excluding oral administration as 94% had chosen to insert it vaginally. No significant difference in pain was found during IUD insertion, nor was healthcare provider ease of insertion significantly different between the two groups. Also, pain was significantly higher before IUD insertion in the misoprostol group.

Oral misoprostol. The impact of cervical priming with oral administration of misoprostol has been evaluated in five placebo-controlled RCTs. In the first trial 35 nulliparous women took misoprostol 400 mcg or placebo orally 90 minutes prior to IUD insertion (Edelman et al., 2011). The procedure also included local anesthesia at the tenaculum site; either benzocaine spray or 1% lidocaine injection. No significant difference in pain or provider ease of insertion was found between the groups.

Esprey et al. (2014) also compared 400 mcg oral misoprostol or placebo in a larger population of nulliparous women (n = 85), but taken two to eight hours before IUD insertion. Highest level of pain was similar between both groups, and providers did not indicate any difference in ease of IUD insertion. Pain scores in the study confirmed that nulliparous women experience considerable pain during IUD insertion.

The third study conducted in nulliparous women (n = 71) evaluating 400 mcg oral misoprostol was conducted by Lathrop et al. (2013). In this study, misoprostol or placebo was taken two to four hours prior to IUD procedure, and those in the misoprostol group reported significantly more pain than those in the placebo group. Nulliparous women reported an approximately two-fold increase in pain compared to multiparous women. Provider perception

of ease of insertion was not significantly different, and the addition of misoprostol did not decrease the need for additional measures such as cervical dilation.

Two RCTS were conducted in mostly parous women to evaluate oral administration of misoprostol for cervical priming. The first aimed to compare sublingual misoprostol 400 mcg and placebo three hours prior to IUD insertion in 89 mostly multiparous women who were having an IUD removed followed by immediate insertion of a new IUD (Heikinheimo et al., 2010). Sublingual misoprostol did not have a significant effect on the ease of insertion. Overall pain experience did not differ between the two groups, yet severe pain and a significant increase in side effects was reported in the misoprostol group. The second RCT evaluating sublingual misoprostol was conducted in 200 parous women delivered by cesarean section and included comparison of 400 mcg misoprostol and 100 mg diclofenac with 100 mg diclofenac orally one hour prior to IUD insertion (Ibrahim & Ahmed, 2013). Adding misoprostol to diclofenac prior to IUD insertion did not result in significant differences in patient-reported pain experienced, and ease of insertion was not significantly different between the two groups.

Non-pharmacological Interventions. In the absence of clear evidence supporting pharmacological interventions, the scope of the appraisal was expanded to include additional strategies used in clinical practice. Additional strategies identified included delayed bladder emptying, aromatherapy, pre-placement counseling, and distraction. Bladder distention causes the uterine axis to become more aligned with the cervical canal which may facilitate easier insertion of an IUD and reduce pain (Cameron, Glassier, Cooper, & Johnstone, 2013). Aromatherapy with lavender oil has anxiolytic properties which may lead to reduced pain (Shahnazi et al., 2012). Psychological preparation before placement may reduce the perception of pain by reducing uncertainty, and information and reassurance of what to expect may lead to a

higher level of pain tolerance (Bahamondes, Mansour, Fiala, Kaunitz, & Gemzell-Danielsson, 2014). During the insertion procedure, distraction provided verbally by the provider or a support person, or from the warmth of a heating pad may reduce the perception of pain (Gemzell-Danielsson et al., 2013).

Delayed bladder emptying. One study proposed use of delayed bladder emptying for management of pain during IUD insertion (Cameron, Glassier, Cooper, & Johnstone, 2013). To determine if IUD insertion is easier in women who have a full bladder at the time of insertion, 200 women with a pre-filled bladder were randomized to either delayed emptying after IUD insertion or immediate emptying before IUD insertion. There was no significant decrease in pain scores between the two groups.

Aromatherapy. Shahnazi et al. (2012) randomized 106 women to inhale ten drops of lavender scent or placebo 30 minutes before IUD insertion. Pain scores after intervention did not show a significant difference between the lavender scent and the placebo groups. However, mean differences of anxiety in both groups was statistically significant showing a positive effect of aromatherapy as complementary treatment.

Pre-placement counseling and distraction. Non-pharmacological interventions aimed at reducing anxiety before and during the IUD placement may be effective at decreasing pain; however, no studies on these approaches have been published to date. Recently published consensus recommendations based on expert opinion stated that non-pharmacological pain management strategies should be used by the provider (Bahamondes et al., 2014). These interventions included pre-placement counseling and the use of distraction during the insertion procedure. The provision of realistic information on what to expect during the procedure, discussion of the variable level of pain women experience, and explanation on the measures that

will be taken to minimize discomfort should occur prior to IUD placement. Other supportive non-pharmacological measures aimed at distraction during the procedure to reduce the perception of pain included the woman concentrating on holding a heating pad suprapubically. A technique called 'vocal local' through conversational distraction by the provider or a support person was one of the most effective ways of decreasing anxiety and pain. As this article is based on expert opinion it was excluded from the critical appraisal.

Implications for Practice

Analgesia. Oral NSAIDs such as naproxen sodium and ibuprofen are widely available; and inexpensive methods of analgesia used successfully in many clinical settings. They require one to two hours to have adequate effect as peak serum levels are attained at one to two hours after administration, with analgesia lasting eight to twelve hours. It is possible that pain may be decreased in the hours after IUD placement. Ketorolac is relatively inexpensive, can be stocked in clinics, and has a wait time of 30 minutes compared with one hour for oral analgesics, with analgesia lasting four to six hours. Logistical considerations might make routine use of ketorolac unrealistic in many clinic settings due to the need for intramuscular injection and a healthcare provider available to administer it, as well as an in-clinic wait time of 30 minutes. Analgesic effects of tramadol (an atypical opioid prescription medication) begin within one hour, reach peak concentration after two to three hours and have a duration of action of four to six hours. It has superior analgesia over NSAIDs and unlike other opioids, has no effects on the respiratory or cardiovascular systems. Nitrous oxide might not reduce IUD insertion pain, but was found to increase satisfaction with pain management during the procedure (Singh et al., 2015). Availability, access, and training for nitrous oxide would need to be addressed in order to offer this form of analgesia for IUD insertion.

Anesthesia. Studies confirmed a lack of efficacy for lidocaine 2% gel in reducing pain with IUD insertion. Physiologically, this intervention would require allowing enough time before IUD insertion based on the pharmacologic properties of the gel, while considering a reasonable time to leave the speculum in place. With adequate time a reduction in pain may occur; however, this is also dependent on how long a patient will tolerate having a speculum in place or having multiple speculum insertions if it is removed after anesthetic administration then replaced for IUD insertion.

The use of a 20 gauge angiocatheter to introduce the 2% lidocaine intracervically provided an innovative delivery mechanism allowing the gel to be placed the length of the cervical canal, but the use of 2% lidocaine did not reduce pain (McNicholas et al., 2012). Administration of a short-acting 4% viscous lidocaine solution five minutes before IUD insertion may be a viable anesthetic for managing IUD insertion-related pain without any apparent safety concerns (Tornblom-Paulander et al., 2015). The viscosity of the formulation of this lidocaine 4% solution minimizes leakage so administration of the anesthetic to the intended tissues is prolonged, leading to reduced pain. The other local anesthetic application, EMLA 5% cream as a topical anesthetic on the cervix before IUD insertion reduced pain after a seven minute wait time (Tavakolian et al., 2015).

Lidocaine 10% spray is a simple and convenient topical anesthetic with minimal side effects. The one study demonstrated a significant reduction in overall procedural pain in the lidocaine treatment group showing it can be effective in reducing pain scores during IUD insertion (Aksoy et al., 2015). Although a pilot study, Nelson and Fong (2013) did not demonstrate any advantage for infusing small amounts of lidocaine into the endometrial cavity to reduce pain associated with IUD insertion. One trial demonstrated lower pain scores after

lidocaine injection (Cirik et al., 2013); however, paracervical anesthesia with lidocaine did not significantly reduce pain in the other two trials (Castro et al., 2014; Mody et al., 2012). Also, participants reported high levels of pain with paracervical block administration which may dissuade providers from this method even if it helps decrease pain during IUD insertion.

Cervical priming. Nitroprusside or nitroglycerin are inexpensive, stable at room temperature, readily available, and have a well-established safety profile with application to mucosal surfaces, but results of the two pilot studies do not support benefit prior to IUD insertion (Bednarek et al., 2013; Micks et al., 2014). Pain scores with IUD insertion are highly variable among women, so a large number of subjects may yield very different results. However, it is unlikely that larger studies would demonstrate benefit as the maximum difference in mean pain scores was less than the 15- to 20- mm difference on a 100-mm visual analog score considered to be clinically significant.

Misoprostol has a short half-life, is stable at room temperature, inexpensive, and the dose can be adjusted. Several aspects of cervical ripening regimens for IUD insertion remain unclear: the minimal dose, timing of administration, and optimal route to obtain the necessary degree of cervical softening before IUD insertion. No study has established a standard on these variables.

Minimal dilation is needed for IUD insertion; therefore, it is likely that the 400 mcg doses administered in the included studies was too high, causing unnecessarily high rates of side effects, mainly pain from uterine cramping. The time for misoprostol to exert its effect on the cervical tissue varies according to the route of administration. When misoprostol is used orally or sublingually, peak concentration occurs in less than 30 minutes, and decreases rapidly thereafter. However, when the vaginal route is used, peak plasma concentration occurs after one hour, there is a gradual decrease with levels remaining high for at least six hours, and at

substantially higher levels than when administered orally. Also, when administered by the vaginal route, side effects of misoprostol are milder and more self-limiting than when taken orally (Scavuzzi et al., 2013).

In only one of the eight trials, the use of misoprostol 400 mcg inserted vaginally by the provider four hours prior to insertion of the IUD was shown to significantly reduce moderate-to-severe pain, and increase ease of insertion in nulligravidas (Scavuzzi et al., 2013). None of the other RCTs demonstrated a significant reduction in patient reported pain with the use of misoprostol for cervical priming prior to IUD insertion. Although there was variation between the studies in route (vaginal or oral) and timing (90 minutes to four hours) of misoprostol administration, the dose (400 mcg) was the same in each study and the overall findings were consistent. Furthermore, in all eight RCTs, premedication with misoprostol was associated with an increase in side effects. Subjects randomized to misoprostol experienced significantly more nausea and uterine cramping (Gemzell-Danielsson et al., 2013).

The studies described covered a wide variety of patients, including nulliparous and multiparas, and women who were having an IUD removed and replaced. Only one RCT demonstrated a clinical benefit to the use of misoprostol for cervical preparation before IUD insertion (Scavuzzi et al., 2013). The authors of the other seven of the RCTs concluded that women should not be routinely premedicated with misoprostol before IUD insertion because the potential harms outweigh the possible benefits (Dijkhuizen et al., 2010; Edelman et al., 2011; Esprey et al., 2014; Heikinheimo et al., 2010; Ibrahim & Ahmed, 2013; Lathrop, Haddad, McWhorter, & Goedken, 2013; Swenson, Turok, Ward, Jacobson, & Dermish, 2012).

Only one study to date specifically addresses the issue of patients who have previously experienced a failed IUD insertion attempt, but was not included in the critical appraisal as it did

not discuss pain (Bahamondes, Espejo-Arce, & Bahamondes, 2015). Researchers determined pretreatment with intravaginal administration of 200 mcg of misoprostol after IUD insertion failure then and four hours before the second attempt of IUD placement was significantly better than placebo at facilitating the insertion of an IUD. Further studies are needed to determine if the benefit of using misoprostol in this specific clinical setting outweighs the risk of side effects.

Non-pharmacological interventions. Evidence for non-pharmacological strategies for the management of pain during IUD insertion was limited. Cameron et al (2013) found that the presence of urine in the bladder does not facilitate easier insertion of an IUD or reduce pain. When lavender was inhaled 30 minutes prior to IUD insertion, pain was not reduced but reduced anxiety was demonstrated (Shahnazi et al., 2012). Anxiety may contribute to higher levels of perceived pain during IUD insertion, so reduction of anxiety is a good strategy to manage pain during the procedure. Although no other studies for the non-pharmacological management of pain during IUD insertion were identified for critical appraisal, expert consensus by Bahamondes et al (2014) is that clinicians should use non-pharmacological pain management strategies. These included psychological preparation prior to IUD placement and a support person to provide distraction during the procedure.

Translation into Guidelines

This project takes an evidence-based approach to provide recommendations for the management of pain during IUD insertion. Evidence was drawn from randomized controlled trials which represent the gold standard for determining efficacy and effectiveness. Although this project provides evidence-based recommendations for the management of pain during IUD insertion, they are not a substitute for clinical judgment. Decisions about care must carefully consider and incorporate the clinical characteristics and circumstances of each individual patient.

Implications for practice are made with an expectation that health professionals will use this evidence with consideration of the context, their clinical judgment, and the patient's preference.

Analgesia. There is currently no evidence to recommend routine prophylactic use of ibuprofen as none of the studies revealed that it reduces insertion-related pain. Data from one RCT suggests that prophylactic use of tramadol or naproxen sodium may reduce pain on IUD insertion (Karabayirli et al., 2012); however, larger follow-up studies are required to confirm these findings. One study supports use of ketorolac, but only for decreasing pain after IUD insertion (Ngo et al., 2015). Nitrous oxide was found to have a rapid onset of action with few adverse effects, and improved patient satisfaction with pain management (Singh et al., 2015).

Anesthesia. There is currently no supporting evidence from RCTs to recommend routine use of local anesthesia for IUD insertions. Lidocaine 2% gel showed no effect on pain with all the studies confirming its lack of efficacy, although one study suggested it may have beneficial effect in women with a history of severe dysmenorrhea (Allen et al., 2013). Other lidocaine formulations may lesson pain during IUD insertion. These include lidocaine 4% applied on the surface of the cervix, in the cervical canal, and into the uterine cavity (Tornblom-Paulander et al., 2015); a lidocaine and prilocaine cream on the cervical opening (Tavakolian et al., 2015); and 10% spray on the cervical surface (Aksoy et al., 2015). Wait times between application and procedure for these formulations to act ranged from three to seven minutes. There is limited evidence supporting routine use of paracervical anesthesia for IUD insertion; however, injectable local anesthesia for lidocaine paracervical block should be on hand for reactive administration when complications arise, such as the need for dilation (Bahamondes et al., 2014).

Cervical priming. There is no clear evidence that cervical priming with nitroprusside, nitroglycerin, or misoprostol reduces pain during IUD insertion. No studies define optimal

misoprostol regimens and there is a lack of data on the clinical usefulness of cervical priming for IUD insertion to reduce pain. In addition, painful uterine cramping is more likely with the use of misoprotol (Gemzell-Danielsson et al., 2013).

Non-pharmacological interventions. The presence or absence of urine in the bladder does not facilitate easier insertion of an IUD or reduce pain (Cameron et al., 2013). Aromatherapy was found to be effective in decreasing anxiety for IUD insertion and may be used as complementary treatment although it may not decrease actual pain (Shahnazi et al., 2012). Counseling should be done prior to IUD placement and include realistic information about what to expect during the procedure, discussion about the variable level of pain that women experience, and explanation of the measures that will be taken to minimize discomfort (Bahamondes et al., 2014). A support person or an assistant to provide distraction during the procedure is effective in reducing anxiety and pain (Bahamondes et al., 2014).

Significance to Advanced Nursing Practice

The IUD is steadily regaining interest among women seeking a highly effective and long-acting reversible contraceptive method. Pain associated with the insertion of an IUD is one barrier to intrauterine contraceptive use; therefore, effective strategies for pain management have the potential to promote the use of IUDs in women who would otherwise opt out of an IUD because of fear of pain at insertion. It is good practice for advanced nurse practitioners (ANPs) to discuss, offer, and use evidence-based interventions for a procedure that may cause pain, such as insertion of an IUD.

ANPs provide frontline care in women's health, including contraception, an essential preventive service, and have an important position in addressing unintended pregnancy. IUDs are supported as first-line contraception for women of all ages, including adolescents (Smith &

Daly, 2011) and provide an additional contraceptive option for ANPs to offer their patients. IUD use has increased nearly five-fold in the last decade (Finer, Jerman, & Kavanaugh, 2012), and 56% of the first 2,500 women enrolled in the Contraceptive CHOICE project selected intrauterine contraception (Secura, Allsworth, Madden, Mullersman, & Peipert, 2010). As more women are being offered and choosing this method, health care providers need updated recommendations for pain control with placement of an IUD.

Dissemination

A manuscript will be prepared for submission to the *Journal of Advanced Nursing.* This journal provides a venue for circulating recommendations for the management of pain during IUD insertion as it is an international, peer-reviewed journal dedicated to addressing aspects of evidence-based nursing. An alternative dissemination plan would include a poster presentation at the annual Alaska Advanced Nursing Practice conference.

Summary

Twenty nine randomized controlled trials from 2010 to 2015 evaluating interventions were critically appraised for managing pain during IUD insertion. Several interventions did not reduce pain; however, a few interventions helped lesson pain. Naproxen decreased pain among parous women and in the first hours afterward in nulliparous women; however, studies showed no benefit of ibuprofen. Tramadol reduced pain in parous women, but only slightly more than naproxen sodium. Lidocaine 4% topical gel in nulliparous women, 10% spray in parous women, lidocaine/prilocaine cream, and 1% paracervical block reduced pain. Misoprostol increased pain and cause more side effects. Inhaled nitrous oxide and aromatheraphy with lavender reduced the anxiety contributing to higher levels of perceived pain during IUD insertion.

Conclusion

Research has shown that long-acting reversible contraceptive methods, including IUDs, are highly effective, and there has been an increase in the use of this type of contraception. Despite the benefits associated with IUDs, one barrier is the fear of pain during the insertion process. Studies emphasized the varying pain women experience with IUD insertion; however, no single intervention was shown to consistently reduce the pain associated with IUD placement. After critical appraisal of the evidence it can be concluded that use of ibuprofen, lidocaine 2% gel, and misoprostol does not reduce pain; however, tramadol, naproxen, lidocaine 4% gel, lidocaine 10% spray, lidocaine/prilocaine cream, and lidocaine injectable block may help in managing IUD insertion-related pain. Other interventions highlighted that reduction of anxiety is a good strategy to attempt to reduce pain during IUD insertion. This project contributes to the body of literature in support of easing the pain of IUD insertion as part of a comparative analysis to assist in the development of guidelines for managing pain during IUD insertion.

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Appendix A

Evidence-based Management of Pain during Intrauterine Device (IUD) Insertion

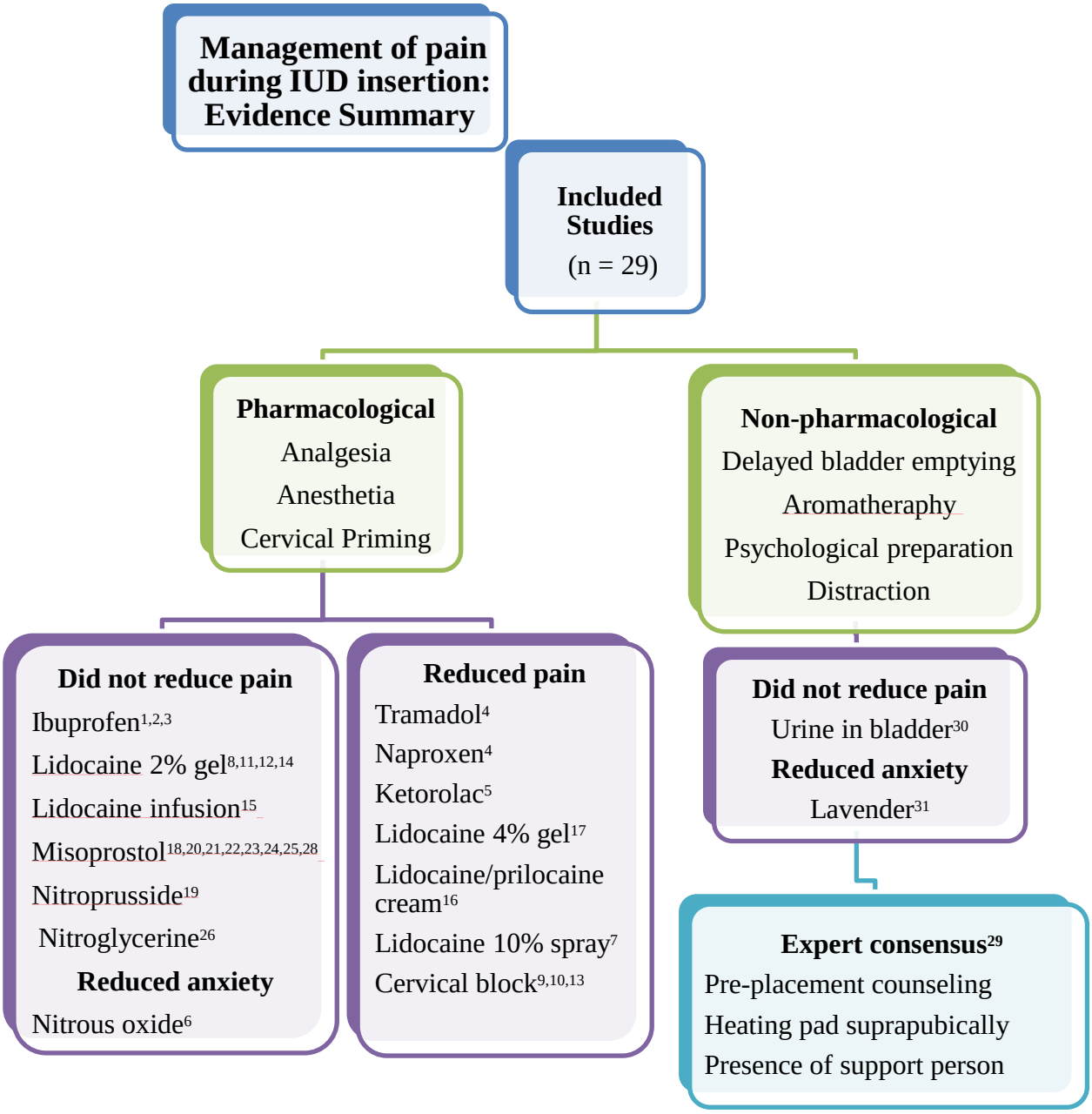

Figure A - 1 *See back for References**

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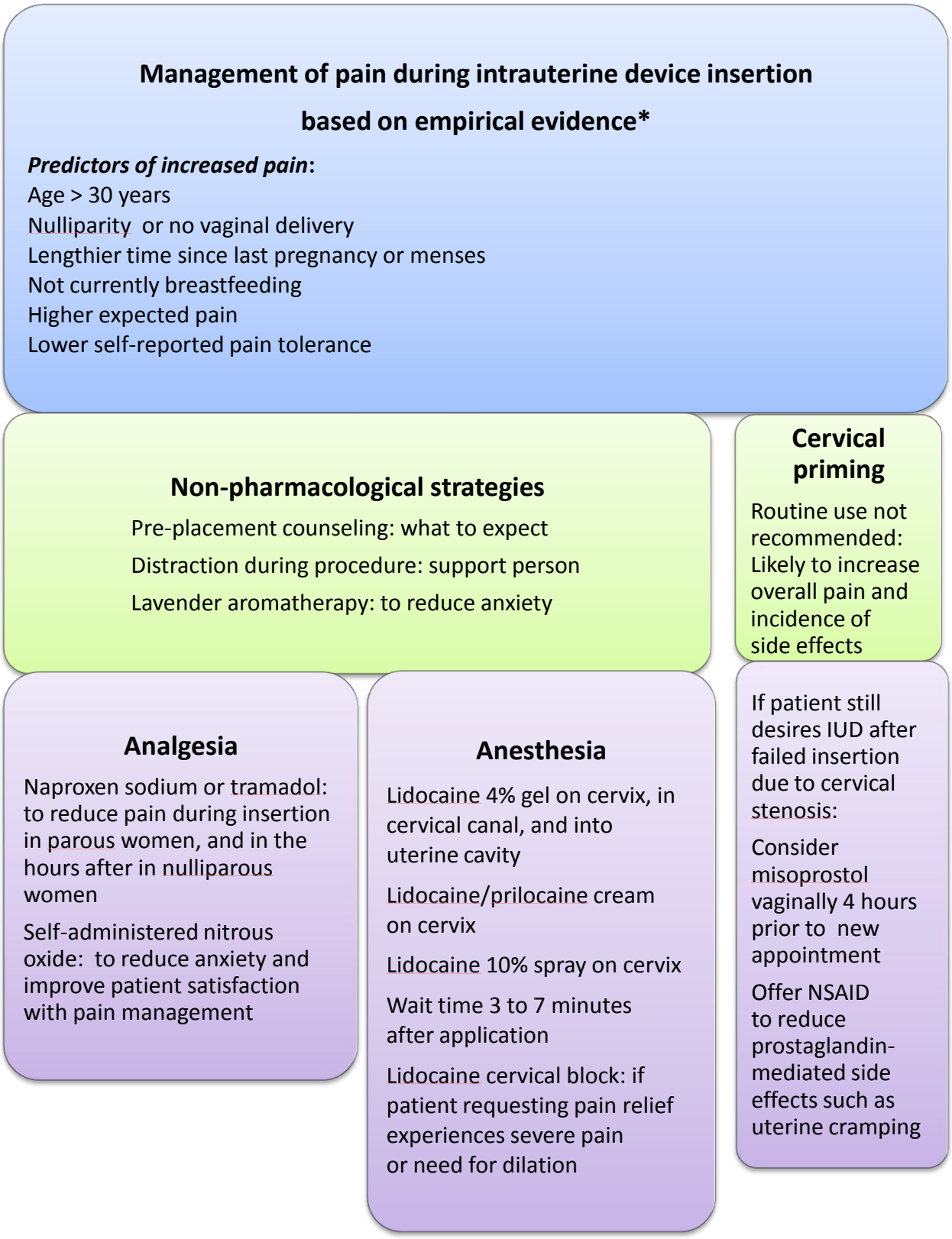
Management of pain during intrauterine device insertion based on empirical evidence*
Predictors of increased pain:
Age > 30 years
Nulliparity or no vaginal delivery
Lengthier time since last pregnancy or menses
Not currently breastfeeding
Higher expected pain
Lower self-reported pain tolerance
Non-pharmacological strategies
Pre-placement counseling: what to expect
Distraction during procedure: support person
Lavender aromatherapy: to reduce anxiety
Cervical priming
Routine use not recommended: Likely to increase overall pain and incidence of side effects
Analgesia
Naproxen sodium or tramadol: to reduce pain during insertion in parous women, and in the hours after in nulliparous women
Self-administered nitrous oxide: to reduce anxiety and improve patient satisfaction with pain management
Anesthesia
Lidocaine 4% gel on cervix, in cervical canal, and into uterine cavity
Lidocaine/prilocaine cream on cervix
Lidocaine 10% spray on cervix
Wait time 3 to 7 minutes after application
Lidocaine cervical block: if patient requesting pain relief experiences severe pain or need for dilation
If patient still desires IUD after failed insertion due to cervical stenosis:
Consider misoprostol vaginally 4 hours prior to new appointment
Offer NSAID to reduce prostaglandin-mediated side effects such as uterine cramping

Figure A - 2

Management of Pain during IUD Insertion based on Empirical Evidence*

Non-pharmacological interventions

- Counseling prior to IUD placement including realistic information about what to expect during the procedure, discussion about the variable level of pain that women experience, and explanation of the measures that will be taken to minimize discomfort.
- A support person or an assistant to provide distraction during the procedure to reduce anxiety and the perception of pain.
- Aromatherapy as complementary treatment to decrease anxiety for IUD insertion.

Analgesia

- There is currently no evidence to recommend routine prophylactic use of ibuprofen.
- Data supports prophylactic use of tramadol or naproxen sodium to reduce pain. Although tramadol exerted superior analgesia, the difference may not be clinically significant as mean pain scores in tramadol and naproxen sodium groups were similar.
- Nitrous oxide has a rapid onset of action with few adverse effects, and improves patient satisfaction with pain management.

Anesthesia

- If a patient requests pain relief, experiences severe pain, or there is a need for dilation, lidocaine cervical block may be injected.
- Lidocaine 2% gel showed no effect on pain with all studies confirming lack of efficacy.
- Other lidocaine formulations may lesson pain during IUD insertion: lidocaine 4% applied on the surface of the cervix, in the cervical canal, and into the uterine cavity; a lidocaine and prilocaine cream on the cervical opening; and 10% spray on the cervical surface.
- Allowing adequate time to elapse is necessary for them to take effect.Wait times between application and IUD insertion ranges from three to seven minutes.

Cervical priming

- There is no benefit for the routine use of misoprostol for cervical priming.
- If the patient still desires an IUD after a failed insertion due to cervical stenosis, consider rescheduling and self-administration of vaginal misoprostol 4 hours prior to the new appointment and offer NSAID to reduce cramping side effects.
- With vaginal route, peak plasma concentrations occur in 1 hour, and at substantially higher levels than when administered orally; side effects are also milder.

Appendix B

Permission to Reproduce Star Model of Knowledge Transformation

From: **Center for Advancing Clinical Excellence** <acestar@uthscsa.edu>
Date: Mon, Aug 10, 2015 at 4:22 PM
Subject: RE: permission to reproduce ACE figure
To: Debra Booysen <dcbooysen@alaska.edu>

Ms. Booysen,

Dr. Stevens has reviewed your request, and you may use it under the fair-use rule, but you will need to give written credit. However, if you are re-publishing the copyrighted material, specific permission is required. Dr. Stevens is the copyright holder and grants you permission to include the model image and a paraphrased description of the model. The image must be accompanied with this phrase: "Copyrighted material (Stevens, 2012). Reproduced with expressed permission" and the bibliographic reference include: Stevens, K. R. (2012). ACE Star Model of EBP: Knowledge Transformation. The University of Texas Health Science Center San Antonio.

Just recently, Dr. Stevens has updated the name of the ACE Star Model to the **Stevens Star Model of Knowledge Transformation** so she has asked me to share this information with you. You may have to update the bibliographic reference to reflect this change. If you have any questions, you may contact Dr. Stevens at stevensk@uthscsa.edu

On another note, our Center is also involved with the Improvement Science Research Network (ISRN). The ISRN's work is to advance the emerging field of improvement science. Our mission is to advance the scientific foundation for quality improvement, safety and efficiency through transdisciplinary research addressing healthcare systems, patient centeredness, and integration of evidence into practice. It provides a laboratory to greatly enhance feasibility and generalizability of NIH (National Institutes of Health) proposals in improvement science. Additionally, it provides an infrastructure for a national program of research to test quality improvement interventions. The ISRN is comprised of national members, the Network Coordinating Center and a Steering Council. Research Priorities were adopted for the ISRN as the best thinking to date about the direction that should be taken in improvement science. Please visit our ISRN website at www.ISRN.net for further details.

Thank you for your interest in improving care and patient outcomes.

Joan Feller
Administrative Assistant Associate
Center for Advancing Clinical Excellence (ACE)
UT Health Science Center San Antonio
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Appendix C

IRB Exempt Approval

Research & Graduate Studies
University of Alaska Anchorage

3211 Providence Drive
Anchorage, Alaska 99508-4614
T 907.786.1099, F 907.786.1791
www.uaa.alaska.edu/research/ric

DATE:	September 13, 2015
TO:	Debra Booysen, MSN
FROM:	University of Alaska Anchorage IRB
PROJECT TITLE:	[800092-1] Management of pain during intrauterine device insertion: development of evidence-based recommendations.
SUBMISSION TYPE:	New Project
ACTION:	DETERMINATION OF NOT RESEARCH
DECISION DATE:	September 13, 2015

Thank you for your submission of New Project materials for this research study. The University of Alaska Anchorage IRB has determined this project does not meet the definition of human subject research under the purview of the IRB according to federal regulations.

We will retain a copy of this correspondence within our records.

If you have any questions, please contact Sharilyn Mumaw at (907) 786-1099 or simumaw@uaa.alaska.edu. Please include your project title and reference number in all correspondence with this office.

Sharilyn Mumaw, M.P.A.

Research Integrity & Compliance Officer

Appendix D

Critical Appraisal Table

APA citation	Critical Appraisal Table
Method	Description of design and how study was carried out
Population	Number and characteristics of patients e.g. nulliparous
Variables (Interventions)	Variables or type of intervention e.g. ibuprofen, lidocaine
Measurement (Method of evaluation of pain)	Scale used to measure outcome variable e.g. VAS
Data Analysis (Significance of pain reduction effect)	Statistics used to answer clinical question
Findings	Statistical or qualitative findings for each statistical test
Appraisal: Worth to Practice	Feasibility of use in ANP practice
Level of Evidence	According to John Hopkins hierarchy of evidence table

Appendix E

Johns Hopkins Hierarchy of Evidence Table

	Strength of the Evidence
Level I	Experimental study/randomized controlled trial (RCT) or meta-analysis of RCT
Level II	Quasi-experimental study
Level III	Non-experimental study, qualitative study, or meta-synthesis
Level IV	Opinion of nationally recognized experts based on research evidence or expert consensus panel (systematic review, clinical practice guidelines)
Level V	Opinion of individual expert based on non-research evidence. (includes case studies, literature review, organizational experience e.g., quality improvement and financial data, clinical expertise, or personal experience)

Note. Newhouse, Dearholt, Poe, Pugh, & White (2005). The Johns Hopkins Evidence-based Practice Rating Scale.

Appendix F

Critical Appraisal Table of Included Studies

Citation	Aksoy, H., Aksoy, U., Ozyurt, S., Acmaz, G., & Babayigit, M. (2015). Lidocaine 10% spray to the cervix reduces pain during intrauterine device insertion: A double-blind randomised controlled trial. *Journal of Family Planning and Reproductive Health Care*, 1-5.
Design/Method	Randomized, double-blind, placebo-controlled trial. Kayseri Education and Research Hospital tertiary family planning clinic, Turkey.
Population	200 parous women aged 19 - 49 years.
Variables/Intervention	Four pumps of 10% lidocaine spray or four pumps of isotonic saline solution spray (three puffs to cervical surface and one puff specifically towards external cervical os) and waited three minutes before insertion.
Measurement	Patient rated pain on a standard continuous 10-cm VAS, from 0 cm (no pain) to 10 cm (worst pain ever).
Data analysis	190 subjects needed to detect clinically significant difference when assuming a power of 80% to detect the primary hypothesis and a type 1 error of 0.05. Normality tested using Shapiro-Wilk test. Variance homogeneity tested using Levene's test. Values expressed as mean±SD or median. Parametric comparisons using Mann-Whitney *U*-test. Statistical significance recognized when $p < 0.05$. Analyses made by G*Power 3.1.7 (Heinrich Heine University, Germany).
Findings	Significantly lower score for overall pain during IUD insertion found in treatment group compared to controls ($p < 0.001$). Control group experienced greater pain than those in treatment group (mean scores 3.23 ± 1.60 vs 1.01 ± 1.20, $p < 0.001$). The frequency of VAS ≥ 4 was statistically significant (41% in controls vs 6% in treatment group, $p < 0.001$). No systemic side effects observed with 10% lidocaine spray.
Worth to practice	Lidocaine spray is a simple and convenient topical anesthetic with minimal adverse effects. Study demonstrated a significant reduction in overall procedural pain in lidocaine treatment group compared with placebo group; shows it can be effective in reducing pain scores during IUD insertion.
Level of evidence	I
Notes	All insertions performed by same gynecologist and team. No nulliparous women.

Citation	Allen, R. H., Raker, C., & Goyal, V. (2013). Higher dose cervical 2% lidocaine gel for IUD insertion: A randomized controlled trial. *Contraception*, *88*, 730-736.
Design/Method	Randomized, double-blind, placebo-controlled trial. University obstetrics and gynecology practice, Providence, RI.
Population	145 nullip and parous women 18 to 49 years.
Variables/Intervention	3 mL of 2% lidocaine gel or placebo gel (KY Jelly) in a 1:1 ratio at the anterior lip of the cervix and 3 mL in the cervical canal for 3 min.
Measurement	Participants rated pain on 0- to 100-mm visual analog scale (VAS).
Data analysis	144 subjects needed assuming an alpha of 0.05, 80% power and a SD of 32 mm to detect a 15-mm mean difference and to minimize a potential Type II error. Chi-square or Fisher's Exact test for categorical variables. Wilcoxon rank sum or *t* test for continuous variables. Association of lidocaine gel with pain on IUD insertion examined by multiple linear regression. Interactions between treatment group and predictors evaluated by an overall *F* test, and Dunnett method. All *p* values two-tailed, with $p < 0.5$ statistically significant. SAS version 9.2.
Findings	Pain with IUD insertion was no different with a mean pain score of 35.2 (median: 34) in the lidocaine group and 36.7 (median: 36) in the placebo group ($p = .8$). No difference even in nulliparous. Lidocaine treatment was associated with a 31.8 point (95% CI: 0.9 - 62.8, $p = .04$) decrease in pain in patients with severe dysmenorrhea. No difference between groups in procedure difficulty as rated by provider. No participants reported any systemic lidocaine side effects.
Worth to practice	Confirms lack of efficacy. Lidocaine gel did not reduce pain, even among nulliparous women. Study showed it may have a beneficial effect in women with a history of severe to very severe dysmenorrhea.
Level of evidence	I
Notes	Provided useful information on predictors of pain: increased pain associated with nulliparity, interval IUD insertion and history of dysmenorrhea. 37 different providers inserted IUDs.

Citation	Bednarek, P. H., Creinin, M. D., Reeves, M. F., Cwiak, C., Esprey, E., & Jensen, J. T. (2015). Prophylactic ibuprofen does not improve pain with IUD insertion: a randomized trial. *Contraception*, *91*(3), 193-197.
Design/Method	Randomized, double-blind, placebo-controlled trial.
Population	202 women, nulliparous or multiparous, 18 years and older.
Variables/Intervention	Oral ibuprofen 800 mg or placebo 30 to 45 min prior to IUD insertion.
Measurement	100-mm visual analog scale to measure pain (0 = no pain, 100 = worst imaginable).
Data analysis	Using a two-sample *t* test, this sample size would provide 80 % power at an alpha of 0.05 to identify a 8-mm difference on a 100-mm VAS assuming a standard deviation of 20 mm. Differences compared using Fisher's Exact test, Chi-squared test or t test. A t test used to evaluate mean pain, reported as median as data not normally distributed. SPSS version 17.0 and SAS software.
Findings	No significant difference; the median pain score was 41.5 mm in the placebo group and 38.0 mm in the ibuprofen group ($p = .50$). Mean and median pain scores did not differe between placebo and ibuprofen when nulliparous or parous were evaluated separately; however, overall median pain scores were 17.5 mm higher in nulliparous women ($p = .004$). Pain decreased in a linear pattern as parity increased from 0 to ≥ 3 in multivariate analysis.
Worth to practice	Ibuprofen 800 mg administered 30 - 45 mins prior to IUD insertion does not decrease pain with IUD insertion. Harms without evidence of benefit include elevated risk of side effects and anxiety about expected pain and increased complexity of scheduling. Study did not address pain in the hours after placement, possible may have decreased pain in the hours following the procedure. Ibuprofen may require 2 h to reach maximum blood levels.Power to evaluate effects for both nulliparous and multiparous women. Sample size was sufficient to detect a difference in VAS score of 14 mm in nulliparous, and a 10 mm in parous women.
Level of evidence	I
Notes	Good discussion of predictors of pain, comparison of nullip versus multip pain levels valuable for project literature review.

Citation	Bednarek, P. H., Micks, E. A., Edelman, A. B., Li, H., & Jensen, J. T. (2013). The effect of nitroprusside on IUD insertion experience in nulliparous women: A pilot study. *Contraception, 87*, 421-425.
Design/Method	Randomized, double-blinded, placebo-controlled pilot study.
Population	24 nulliparous aged 18 to 45 years.
Variables/Intervention	Nitroprusside 10 mg compounded into a 1 % aqueous gel or placebo intracervically immediately prior to IUD insertion.
Measurement	100-mm visual analog scale (VAS; 0 = no pain, 100 mm = worst imaginable pain). Technique standardized with use of 2 mL lidocaine into tenaculum site.
Data analysis	Group sizes of 12 each to achieve 82 % power to detect a 30-mm difference between groups and a one-sided α of 0.05 given a pooled standard deviation of 28 mm. Fisher's Exact test, χ^2 test or *t* test to compare baseline differences. Repeated-measures approach for comparing outcomes on VAS. Mena VAS scores presented.
Findings	A 15 - 20 mm reduction in the VAS score is considered clinically important. No significant differences between mean pain scores at IUD insertion (mean = 74 mm, SD = 18 for placebo, mean = 61 mm, SD = 26 for nitroprusside, $p = 0.18$) or for any other time during the procedure. Mean satisfaction score with pain control was 64.5 mm in the nitroprusside group versus 82.4 mm in the placebo group ($p = .20$). Provider insertion difficulty on the VAS was similar in the two groups (26.5 ± 27.3 for placebo and 32.4 ± 22.7 for nitroprusside group, $p = .57$).
Worth to practice	Intracervical administration of 10 mg nitroprusside gel immediately before IUD insertion does not provide a clinically relevant reduction in pain with IUD insertion in nulliparous women. Pilot study showing a 14 mm difference in mean pain scores which is less than the 15 to 20 mm considered to be clinically significant. Results from this pilot study do not support benefit for intracervical nitroprusside.
Level of evidence	I
Notes	Small exploratory study, this intervention may raise concern of harm and does not support benefit of nitroprusside.

Citation	Castro, T. V., Franceschini, S. A., Poli-Neto, O., Ferriani, R. A., Silva de Sa, M. F., & Vieira, C. S. (2014). Effect of intracervical anesthesia on pain associated with the insertion of the levonorgestrel-releasing intrauterine system in women without previous vaginal delivery: A randomized controlled study. *Human Reproduction, 29*(11), 2439-2445.
Design/Method	Randomized, open, parallel-group clinical trial. Clinics Hospital of the Medical School of Rebeirao Preto, Brazil.
Population	100 women, nulliparous or without previous vaginal delivery.
Variables/Intervention	400 mg ibuprofen one hr prior to insertion or 1.8 mL of 2% lidocaine to cervix equally divided among four injection sites 5 min before IUD insertion.
Measurement	Visual analog scale (VAS) 0 = no pain, 100 = worst pain imaginable; qualitatively analyzed (0 - 30 mm: mild pain, 40 - 60 mm: moderate pain and 70- 100 mm: severe pain). Ease of insertion rated as easy of difficult.
Data analysis	80 subjects required, alpha of 5% and test power of 80%, considered a 10% difference to achieve clinical relevance. Chi-squared test for qualitative variables, Student's *t* test for normally distributed quantitative variables. Linear mixed-effects model to evaluate paired variables. Logistic regression performed for covariates. Level of significance set at 5%. SAS 9.0 software.
Findings	Pain , level of discomfort, and difficulty of insertion did not differ between the groups. Difference between mean pain level in intracervical anesthetic group and NSAID group was < 10%. Intracervical anesthesia reduces moderate/severe pain by 40% [adjusted OR: 0.6 (95% CI: 0.2 - 1.4)] but without statistical significance.
Worth to practice	Use of injectable intracervical anesthetic compared with NSAID is not associated with pain relief. Pain no different when injectable intracervical anesthetic or NSAID used in nulliparous women or in those without previous vaginal delivery. Although statistically insignificant, intracervical anesthesia reduced the risk of moderate/severe pain by 40% compared with the use of a NSAID.
Level of evidence	I

Citation	Chor, J., Bregand-White, J., Golobof, A., Harwood, B., & Cowett, A. (2012). Ibuprofen prophylaxis for levonorgestrel-releasing intrauterine system insertion: a randomized controlled trial. *Contraception, 85*, 558-562.
Design/Method	Randomized, double-blind, placebo-controlled trial. University of Illinois Medical Center.
Population	81 nulliparous or parous women, 18 years and older.
Variables/Intervention	800 mg ibuprofen or placebo 45 min prior to IUD insertion.
Measurement	10-cm visual analog scale (VAS, endpoints 0 = no pain and 10 = unbearable. Providers completed short questionnaire on experience with ease of insertion and need for dilation.
Data analysis	Sample size of 37 participants in each group to detect a difference of 1.5 cm in the VAS assessment of pain with a 80% power and an alpha of 0.05. Mean pain data using χ^2 for categorical data and *t* test or Wilcoxon signed-rank test for continuous data using a two-tailed *p* value of .05. SAS version 9.2.
Findings	Mean pain scores at time of IUD insertion did not differ significantly between the placebo and ibuprofen groups (3.34 vs. 3.69 respectively; *p* = .91.
Worth to practice	Results are consistent with two trials that also failed to find a difference in pain at time of insertion between women who received ibuprofen or placebo. Pain of IUD insertion similar between women who received either ibuprofen or placebo. Mean interval from premedication with ibuprofen to insertion was 43 min; possible that medication was not given long enough prior to IUD insertion to have adequate effect (peak serum levels attained at 1-2 h after administration).
Level of evidence	I
Notes	No significant differences in distribution of practitioner type, resident physicians placed 80% of IUDs. Mean insertion pain levels in both study groups (3.3 with placebo and 3.9 with ibuprofen) were higher than level reported by Hubacher et al (2006).

Citation	Cirik, D. A., Taskin, E. A., Tuglu, A., Ortac, A. S., & Dai, O. (2013). Paracervical block with 1% lidocaine for pain control during intrauterine device insertion: A prospective, single-blinded, controlled study. *International Journal of Reproductive Contraception Obstetrics and Gynecology*, *2*(3), 263-267.
Design/Method	Prospective, single-blinded, controlled study
Population	95 women aged 18-45 years nulliparous and parous
Variables/Intervention	10 mL 1% lidocaine paracervical block or 10 mL 0.9% NaCl paracervically injected as placebo, or no analgesia before IUD insertion.
Measurement	Visual pain scale with no pain graded as 0 and the worst pain ever as 10.
Data analysis	SPSS version 13.0. Demographic variables compared with either ANOVA or Kruskal-Wallis tests. The Chi-square test for categorical variables. Tukey correlation analysis done with Spearman's correlation test. Significance level set at p value < 0.05.
Findings	Median pain scores during IUD insertion were 2, 6, and 6 respectively, in the paracervical block, placebo, and no treatment groups. Pain scores in the paracervical block group were significantly lower (p = 0.001)
Worth to practice	Paracervical block is an easy, safe, and effective method of pain control during IUD insertion.
Level of evidence	I
Notes	Compares block with placebo as well as with no intervention.

Citation	Dijkhuizen, K., Dekkers, O. M., Holleboom, C. A., De Groot, C. M., Hellebrekers, B. W., Van Roosmalen, G. J., … Helmerhorst, F. M. (2010). Vaginal misoprostol prior to insertion of an intrauterine device: A randomized controlled trial. *Human Reproduction, 26*(2), 323-329.
Design/Method	Double-blinded multicenter randomized controlled trial Outpatient gynecology department, the Netherlands
Population	199 nulli- and parous ≥ 18 years women included
Variables	400mcg misoprostol inserted vaginally or placebo 3h before IUD insertion.
Measurement	Visual analog scale (VAS) scale 'no pain' to 'worst imaginable pain' in millimeters, validated pain scale (Sriwantanakul et al., 1983). Difficulty of IUD insertion measured on 10-point scale 0 = extremely easy and 10 as extremely difficult. Completed directly after insertion.
Data analysis	Sample size of 266 based on type 1 error of 0.05 and a power of 0.80. Power to detect side effects was 0.44. Pain scores and difficulty of insertion given as mean ± SD and compared using unpaired *t* tests. Statistical package for the Social Sciences, version 14.
Findings	Mean pain scores were similar in both groups; 46mm in the misoprostol group, and 40mm in the placebo group ($P = 0.14$). Difficulty of insertion did not differ 2.9 versus 2.8 in the misoprostol and placebo group ($P = 0.77$). However, nulliparous participants pain scores were higher (57) than multiparous (30) participants, irrespective of the medication group ($P = 0.001$), and difficulty of insertion was also different between the two groups: 2.2 for multiparous versus 3.5 for nulliparous ($P = 0.001$). Side effects (most commonly abdominal cramping) significantly more frequent in misoprostol group 56 (56.6%) compared to 39 (42.4%) in the placebo group ($P = 0.05$, RR 1.3, 95% CI 1.0 - 1.7).
Worth to practice	Pain during IUD insertion was not influenced by pretreatment with misoprostol. Also, it did not reduce the number of failed insertions. Routine administration of misoprostol prior to IUD insertion is ineffective and might even cause side effects.
Level of evidence	1
Notes	Inserted by interns, residents, midwives, gynecologists. Primary outcome measure was proportion of failed IUD insertions. Interestingly researchers reported pain scores as generally low when they were 40 to 44mm! Discusses doses and routes.

Citation	Edelman, A. B., Schaefer, E., Olson, A., Van Houten, L., Bednarek, P., Leclair, C., & Jensen, J. T. (2011). Effects of prophylactic misoprostol administration prior to intrauterine device insertion in nulliparous women. *Contraception, 84*, 234-239.
Design/Method	Double-blind, randomized, placebo-controlled study Oregon Health and Science University
Population	35 nulliparous aged 18 to 45 years.
Variables/Intervention	Misoprostol 400 mcg or placebo taken buccally 90 min prior to appointment time. Included local anesthesia at tenaculum site (benzocaine spray or 1 - 2 mL of 1% lidocaine injected).
Measurement	Subjects rated pain using 100 mm VAS (anchors 0 = none, 100 mm = worst imaginable at several time points. Providers recorded ease of insertion using VAS (anchors 0 = easy, 100 mm = extremely difficult).
Data analysis	80% power at an α of 0.05 (one-sided for pain outcomes). Categorical and continuous data analyzed using χ^2 and Student's *t* tests, respectively. SPSS software, version 17.
Findings	No significant difference in reported pain [misoprostol mean 65 mm (SD 21), placebo 55 mm (21), p = 0.83]. Provider-reported ease of placement was not significantly different between groups [misoprostol mean 24 mm (SD 19), placebo 29 mm (21), p = 0.5]. Subjects in misoprostol group reported more symptoms of nausea (misoprostol 47%, placebo 5%, p = 0.05), and cramping (misoprostol 47%, placebo 16 %, p = 0.04).
Worth to practice	Routine use of misoprostol does not reduce the pain a woman experiences, improve the ease of insertion for providers, or impact overall likelihood of successful placement. Women premedicated with misoprostol experience more adverse effects than benefits. The benefits of misoprostol do not outweigh the disadvantages, does not increase the likelihood of successful insertion, and does not reduce the pain associated with insertion.
Level of evidence	1
Notes	Since routine misoprostol does not improve outcomes and is associated with some proven and theoretical harms, the practice cannot be recommended for IUD insertion

Citation	Esprey, E., Singh, R. H., Leeman, L., Ogburn, T., Fowler, K., & Greene, H. (2014). Misoprostol for intrauterine device insertion in nulliparous women: A randomized controlled trial. *American Journal of Obstetrics and Gynecology, 210*, 208.e1-5.
Design/Method	Randomized controlled double-blind trial University of New Mexico reproductive health clinic
Population	85 nulliparous of any age (3 ineligible) total 82 Computer generated 8-block randomization sequences
Variables/Intervention	400mcg buccal or placebo 2-8 hours before insertion.
Measurement	VAS pain scale 0 = none and 10 = worst imaginable pain, baseline, immediately after insertion, and before discharge from clinic. VAS scale (0 = easy and 10 = extremely difficult) for providers to rate ease of insertion.
Data Analysis	Power of 80% and $\alpha = 0.05$ (2-tailed) with a sample size of 80. Fisher exact test for categorical and *t* test for continuous variables. Statistical significance set at $P \leq .05$. SAS statistical software version 9.3.
Findings	Highest level of pain immediately after insertion was similar between the misoprostol (5.8 ± 2.0) and placebo (5.9 ± 2.0) groups ($P = .94$). The pain was described the pain as moderate, 50% in the misoprostol group and 40% in the placebo group ($P = .6$). Providers did not indicate any difference in ease of IUD insertion with a mean score of 2.2 ± 2.2 in the misoprostol group and 2.5 ± 2.2 in the placebo group ($P = .54$).
Appraisal/Worth to practice	No reduction in pain between women with 400 mcg of pre-procedure misoprostol, and no differences in provider perceptions of ease of insertion. Confirms IUD insertion is a painful procedure. Routine use of misoprostol in nulliparous women does not reduce pain with insertion or improve the ability to insert an IUD.
Notes	Providers were physicians skilled in IUD insertion. Also included 4-point Likert scale for patient preference for having IUD placed without delay for a med to decrease insertion pain (go to p.208e3 if want to include these results). Discussion of barriers.
Level of evidence	1

Citation	Heikinheimo, O., Inki, P., Kunz, M., Parmhed, S., Anttila, A., Olsson, S., ... Gemzell-Danielson, K. (2010). Double-blinded, randomized, placebo-controlled study on the effect of misoprostol on ease of consecutive insertion of the levonorgestrel-releasing intrauterine system. *Contraception*, *81*, 481-486.
Design/Method	Double-blinded, randomized, placebo-controlled study. Subset of larger trial at 17 clinics in Finland, France, Ireland, and Sweden.
Population	89, mostly parous, aged 23 to 45 years, opting for immediate replacement of IUD after 4y and 3 to 9mo.
Variables/Intervention	400 mcg misoprostol or placebo sublingually 3 h before insertion.
Measurement	Pain by the patient rated as none, mild, moderate or severe. Ease of insertion by investigator rated as easy of difficult.
Data analysis	Sample size of 86 chosen based on statistical considerations (assumed proportion of easy insertions of 0.99 in the misoprostol and 0.79 in the placebo group), power of 80%. Means and SDs for continuous variables and frequency counts for categorical data. Fisher's Exact test for difficulty or ease of insertion. Significant when two-sided p value $\leq .05$.
Findings	Women who received misoprostol did not report less pain than those who received placebo. No or mild pain was experienced by 16 (37.2%) and 16 (34.8%) receiving misoprostol and placebo, respectively. Severe pain was reported by 10 (23.3%) in the misoprostol group and by 5 (10.9%) in the placebo group. Sublingual misoprostol did not have a significant effect on the ease of insertion ($p = 1.00$) and the overall pain experience did not differ between the two groups; more severe pain was reported following misoprostol. Adverse events (oral pain, nausea and diarrhea, or uterine contractions) were seen in significantly more women treated with misoprostol ($n = 22$) than with placebo ($n = 5$)(51.2% vs. 10.9%).
Worth to practice	Study results do not support routine use of misoprostol to facilitate IUD insertion. Cervical priming with sublingual misoprostol 3 h prior to insertion did not result in improvement in ease of insertion, and there was no difference in pain between the misoprostol and placebo groups, yet severe pain was reported more frequently in the misoprostol group.
Level of evidence	1
Notes	11 well experienced and trained providers. Evaluated insertion immediately after removal of first IUD where may be increased risk for difficult insertion after long-term use of LNG-IUD (as with perimenopausal or nulliparous women). Main outcomes were ease or difficulty of insertion.

Citation	Ibrahim, Z. M., & Ahmed, W. A. (2013). Sublingual misoprostol prior to insertion of a T380A intrauterine device in women with no previous vaginal delivery. *The European Journal of Contraception and Reproductive Health Care, 18*, 300-308.
Design/Method	Single-blind randomized controlled trial. Gynecology Clinic of Suez Canal University Hospital, Egypt.
Population	200 parous women delivered by cesarean section.
Variables/Intervention	400 mcg misoprostol sublingually and 100 mg diclofenac potassium orally or only 100 mg dicolofenac orally one hour prior to insertion.
Measurement	Visual analog scale (VAS) 0 to 10, 0 = no pain, and 10 = worst possible pain imaginable. Insertion classified by investigator as 'easy', 'usual', 'difficult', or 'failed'.
Data analysis	Mean values, standard deviations, frequencies, and percentages. Student's *t* test and analysis of variance for significance of difference, Chi-squared test for categorical data. A probability value less than 0.05 was considered statistically significant. Microsoft Excel 2003 and SPSS version 15.
Findings	There were no significant differences in patient-reported pain experienced at IUD insertion. VAS pain estimation for diclofenac + misoprostol group median was 7 (2.5 - 10) and for the control group was 6.5 (0 - 10); $p = 0.8$. Ease of insertion was not significantly different between the two groups. Nausea was the most frequent side effect noted in 19.7 % of women in the diclofenac + misoprostol group, as compared to only 4.4 % of those pretreated solely with diclofenac. (see table pg 304 to add significance for headache and cramping)
Worth to practice	IUD was given only one hour after sublingual misoprostol intake. "Adding sublingual misoprostol to diclofenac may cause side effects without providing the benefit of an easier and/or more successful insertion" (p. 307). Routine pretreatment with misoprostol is not recommended.
Level of evidence	1
Notes	All gynecologists with at least three years experience inserting IUDs. Primary outcome measure was success of failure of insertion. Secondary outcome measures were ease of insertion and pain.

Citation	Karabayirli, S., Ayrim, A. K., & Muslu, B. (2012). Comparison of the analgesic effects of oral tramadol and naproxen sodium on pain relief during IUD insertion. *The Journal of Minimally Invasive Gynecology*, *19*(5), 581-584.
Design/Method	Randomized, double-blinded, clinical trial. University-affiliated hospital, single-center.
Population	103 multiparous women aged 18 to 49 years.
Variables/Intervention	Oral tramadol 50 mg (n = 35) or naproxen sodium 550 mg (n = 34) or placebo (n = 34) one hour before IUD insertion.
Measurement	10 point visual analog scale with a score of 10 meaning the "worst imaginable pain".
Data analysis	Sample size each group 29, with a power of 80 % and an α of 0.05. Software used included SigmaXL version 6.1, Power and Sample Size Calculations for a One-Way ANOVA, and SPSS version 17.0. Tested for normality using Kolmogorov-Smirnov test with a Lilliefors significance correction. Differences analyzed using analysis of variance. Homogeneity calculated using Levene test. Posthoc analysis using Tukey honestly significantly different post hoc test. The χ^2 or Fisher exact test to analyze categorical variables. Data given as mean (SD) and *p* value of < .05 considered significant.
Findings	VAS scores were significantly different between the 3 groups (*p* = .001). Pain scores in the tramadol group were significantly lower than in the naproxen group (*p* = .001), and scores in the naproxen group were significantly lower than in the placebo group (*p* = .001). The mean (SD; 95% CI) VAS pain score of 2.31 (0.60; 2.09-2.53) in the tramadol group was significantly lower than in the naproxen group (2.94 [0.71; 2.69-3.18]) and the placebo group (4.88 [1.0; 4.54-5.22]).
Worth to practice	Tramadol 50 mg demonstrated superior analgesia over naproxen and placebo during IUD insertion. Naproxen demonstrated significantly lower mean pain scores than placebo. Oral administration of naproxen 550 mg or Tramadol 50 mg orally one hour prior to IUD insertion can be used to relieve pain; however tramadol is more effective.
Level of evidence	I
Notes	When tramadol and naproxen were compared, the tramadol mean scores were significantly lower, although this may not be clinically significant as the pain scores in both groups were similar. Study does not take into account nulliparity.

Citation	Lathrop, E., Haddad, L., McWhorter, C. P., & Goedken, P. (2013). Self-administration of misoprostol prior to intrauterine device insertion among nulliparous women: A randomized controlled trial. *Contraception, 88*, 725-729.
Design/Method	Double-blind, randomized, controlled trial.
Population	71 nulliparous 18 years or older.
Variables/Intervention	400 mcg misoprostol or placebo bucally 2 - 4 h prior to procedure appointment time.
Measurement	Pain score using 100-mm validated visual analog scale (0 = none, 100 mm = worst imaginable). Provider rated ease of insertion on 100-mm scale (0 = extremely easy, 100 mm = impossible).
Data analysis	80% power to detect a mean difference of at least 16 mm in participant-reported pain using VAS with an α of .05 assuming 23-mm standard deviation. Chi-squared analysis of Fisher's Exact Tests to detect differences for categorical variables. Mann-Whitney to sompare medians for continuous variables. Descriptive statistics using SPSS version 20.
Findings	Patients in the misoprostol group reported significantly more pain than those in the placebo group immediately before (p = .0001) and after (p = .044). IUD insertion median and range of perceived ease of insertion reported by providers for the misoprostol group was 21 mm (0 - 100) and 21 mm (0 - 68) for the placebo group which was not significantly different (p = .75).
Worth to practice	Misoprostol increased reported pain with and after IUD insertion and did not decrease provider perception of ease of insertion of IUDs in nulliparous women, and should not be recommended routinely for cervical priming prior to nulliparous IUD insertion.
Level of evidence	1
Notes	All obstetrician gynecologists with extensive family planning training.

Citation	Maguire, K., Davis, A., Rosario Tejeda, L., & Westhoff, C. (2012). Intracervical lidocaine gel for intrauterine device insertion: A randomized controlled trial. *Contraception*, *86*, 214-219.
Design/Method	Randomized, double-blind, placebo-controlled trial. Columbia University medical Center, New York.
Population	200 women, aged 18 to 45 years, nulliparous and parous.
Variables/Intervention	2% lidocaine gel or matching placebo gel (Surgilube) soaked onto a cotton swab and inserted into the cervix up to the internal os for 60 secs.
Measurement	Participants rated pain on a 100- mm VAS.
Data analysis	110 women needed assuming two-sided alpha of 0.05 and 90% power. 200 particpants allowed 80% to detect a 20- mm difference on the VAS. Used *t* tests or Wilcoxon-Mann-Whitney tests to evaluate pain scores. Linear regression to examine predictors of pain. SAS 9.2 statistical software.
Findings	Pain scores were comparable in both groups: mean 50.9 mm (SD 32) for the lidocaine group and 51.0 mm (SD 31) for the placebo groups (p = .98). Stratified for parity, stratified analysis showed no treatment effect.
Worth to practice	No significant difference in mean pain with intracervical lidocaine gel compare to placebo, whether nulliparous or parous. Two percent lidocaine did not decrease IUD insertion pain.
Level of evidence	I
Notes	Multivariate analyses identified longer time since last pregnancy, lower parity, higher anticipated pain, and dysmenorrhea as predictors of pain.

Citation	McNicholas, C. P., Madden, T., Zhao, Q., Secura, G., Allsworth, J. E., & Peipert, J. F. (2012). Cervical lidocaine for IUD insertional pain: a randomized controlled trial. *American Journal of Obstetrics and Gynecology, 207*, 384.e1-6.
Design/Method	Randomized, double-blind, controlled trial. Washington University.
Population	199 women aged 18 to 45 years, equal number of nulliparous and parous women.
Variables/Intervention	0.5 - 1 mL of 2% lidocaine gel to ectocervix at planned tenacum site, 2 - 3 mL via 20G angiocatheter into endocervical canal 3 mins prior to insertion of IUD.
Measurement	10- point visual analog scale.
Data analysis	Mean pain score of 4 (SD = 2.5) for women undergoing IUD insertion found in preliminary data from the Contraceptive CHOICE project. 50% reduction in the mean pain score considered clinically important. Required 86 women to reach 90% power with an alpha (type 1) error of 0.05. SAS 9.2 software. Significance set at $p < .05$. Continuous variables summarized as means, medians, ranges, and SD. Categorical variables presented as frequencies. Continuous variables analyzed with Student *t* test. χ^2 and Fisher exact tests to analyze categorical variables. Pain scores not normally distributed, analyzed using Wilcoxon rank sum test.
Findings	Insertional pain scores between nulliparous and parous women were significantly different regardless of intervention. Median pain score in placebo was 7 among nulliparous women and 5 among parous women, and in the lidocaine group median pain was 6 in nulliparous women and 4 in parous women. No difference in insertional pain between the placebo and lidocaine groups: median pain score was 6 in placebo arm and 5 in the lidocaine arm ($p = .20$).
Worth to practice	Despite the finding that nulliparous women had significantly higher pain scores, reported pain was not different for nulliparous women randomized to intracervical lidocaine. Innovative delivery mechanism using angiocatheter allow gel to be placed the length of the cervical canal. Physiologically plausible intervention allowing 3 mins before insertion: time chosen based on pharmacologic properties of the gel and reasonable amount of time to leave speculum in place. With more time may see an improvement of pain scores but how long will patient tolerate having speculum in place or having multiple speculum exams if removed after anesthetic administration then replaced for IUD insertion.
Level of evidence	I
Notes	All participants received ibuprofen approximately 10 mins prior to procedure to minimize postprocedure cramping.

Citation	Micks, E. A., Jensen, J. T., & Bednarek, P. H. (2014). The effect of nitroglycerin on the IUD insertion experience in nulliparous women: A pilot study. *Contraception*, *90*(1), 60-65.
Design/Method	Randomized, double-blinded, placebo-controlled pilot study.
Population	24, mostly nulliparous.
Variables/Intervention	Nitroglycerin 0.5 mg gel (1 mL) or placebo gel applied vaginally 30 min prior to IUD placement.
Measurement	Participants rated their pain using a 100-mm visual analog scale (0 mm = no pain, 100 mm = most pain imaginable). Providers rated ease of insertion using the 100-mm VAS (0 mm = very easy, 100 mm = very difficult).
Data analysis	Mean and standard deviation reported, all *p* values calculated using Fisher's Exact test or Student's *t* test.
Findings	The mean pain score with IUD insertion was 55 mm [standard deviation (SD) = 29.7 mm] in the placebo group and 57.4 mm (SD 22.1 mm) in the nitroglycerin group ($p = .82$). No difference in ease of insertion reported by providers.
Worth to practice	Results do not support the use of nitroglycerin prior to IUD insertion. Vaginal administration of 0.05 mg nitroglycerine gel 30 minutes prior to IUD insertion does not appear to decrease patient reported pain among nulliparous women or ease insertion for providers.
Level of evidence	1
Notes	Possible that time interval between nitroglycerine application and IUD insertion or dose of medication was not sufficient to show a beneficial effect, although prolonged interval or higher doses may cause more side effects, may not be practical, or acceptable to the provider or the patient. Pilot study, small number of participants, provides exploratory data. Subjects had the option of taking ibuprofen prior to the procedure; may be an important cofounder, since it was taken by more subjects in the nitroglycerin group.

Citation	Mody, S. K., Kiley, J., Rademaker, A., Gawron, L., Stika, C., & Hammond, C. (2012). Pain control for intrauterine device insertion: A randomized trial of 1% lidocaine paracervical block. *Contraception*, *86*, 704-709.
Design/Method	Randomized controlled trial, blok randomization stratified by parity. Northwestern Medical Faculty Foundation practice (single clinical site), Chicago, IL.
Population	50 nulliparous and multiparous women.
Variables/Intervention	2 mL 1% lidocaine at tenaculum site and 10- mL paracervical anesthetic, 3 min waiting period prior to insertion, or no analgesia (saline injection not used as a control as researchers wanted to compare block to standard of care).
Measurement	Participants rated pain on visual analog scale graded 0 (no pain) to 10 (worst pain). Providers not blinded. Senior resident, advanced practice nurses, or attending physician inserted IUDs. Potential side effects (metallic taste and tinnitus) recorded.
Data analysis	Sample size of 38 needed calculated based on a 20- mm difference on VAS to be clinically significant, 80% power. Two-tailed test and type 1 error rate of 5% assumed. Independent-sample *t* test for continuous data or Fisher's Exact Test for dichotomous data. Wilcoxon rank sum test used since data were non-normal. Data reported as percentages, means with standard deviations and 95% confidence intervals (CI) or medians.
Findings	Lower median pain score in paracervical block group (24 mm) compared with no analgesia (62 mm) during IUD insertion, but not statistically significant ($p = .09$). Statistically significant decrease in pain during tenaculum placement ($p = .008$) when local administered at 12'clock. Standard deviation was 27.5 mm in no analgesia group and 35.9 mm in paracervical block group.
Worth to practice	Study showed large standard deviation for pain scores emphasizing that patients have varying pain with IUD insertions and methods to alleviate pain are worthwhile. Some participants did report high levels of pain with paracervical block administration (median 40.0) which may dissuade providers and patients from using it even if it helps decrease pain during IUD insertion (median pain with block was lower).
Level of evidence	I
Notes	Provided data and insight regarding specific characteristics associated with pain during IUD insertion: more pain in multiparous women with fewer vaginal deliveries and greater time since last pregnancy, low pain associated with breastfeeding and higher gravidity.

Citation	Mohammad-Alizadeh-Charandabi, S., Seidi, S., & Kazemi, F. (2012). Effect of lidocaine gel on pain from copper IUD insertion: A randomized double-blind controlled trial. *Indian Journal of Medical Sciences*, *64*(8), 349-355.
Design/Method	Randomized, controlled, clinical trial. Public health center, Iran.
Population	Aged 18 to 49 years
Variables/Intervention	Intracervical lidocaine gel, lubricant gel, or no intervention.
Measurement	Visual analog scale measured from 0 = no pain to 10 = worst imaginable pain.
Data analysis	96 subjects needed to detect 20% reduction in pain with to-sided 5% significance level and power of 90%. One-way ANOVA and Kruskal-Wallis for quantitative variables. Linear regression to determine effect of lidocaine, $p < .05$ considered significant. SPSS/13 statistical software.
Findings	Mean pain score was 3.5, approximately half (46%) reported moderate pain. No statistically significant difference in mean pain scores between the 3 groups: 3.4 in lidocaine gel group, 3.4 in the lubricant gel, and 3.7 in the no intervention group.
Worth to practice	2% lidocaine gel did not significantly reduce IUD insertion pain. Gel was used intracervically, not on the outer part of the cervix where tenaculum placed.
Level of evidence	I
Notes	Article provides discussion on pain pathways relating to IUD insertion.

Citation	Nelson, A. L., & Fong, J. K. (2013). Intrauterine infusion of lidocaine does not reduce pain scores during IUD insertion. *Contraception*, *88*, 37-40.
Design/Method	Randomized, double-blind, placebo-controlled, investigator-funded pilot study. Women's Health Care Clinic, Los Angeles Biomedical Research Institute at Harbor-UCLA Medical Center.
Population	40 women.
Variables/Intervention	1.2 mL of 2% lidocaine or normal saline infused 3 min prior to IUD insertion using a Pipet Curet endometrial aspirator with a 4- mm outer diameter into 3 parts of endometrial cavity: lower one third, middle and top of cavity. Two experienced clinicians.
Measurement	Participants rated pain on a scale of 0 (no pain) to 9 (worst pain in life).
Data analysis	Sample size selected arbitrarily for convenience due to budget and time constraints. Would need 418 subjects to detect a significantly significant difference in pain scores, assuming an 80% power and a 5% alpha error. Statistical significance calculated using *t* test to compare means of continuous variables with $p < .05$ as the level of significance.
Findings	Mean pain scores did not differ between the lidocaine group (mean score 3.0) and the normal saline group (mean score 3.7) ($p = .40$). Eleven of the women took NSAIDs before insertion, but their mean pain scores (3.89) did not differ significantly from those who did not take NSAIDs (3.25) ($p < .76$). Mean pain scores who had lidocaine and NSAIDs (3.8) did not differ from those who received normal saline and had no NSAIDs (3.7) ($p = .86$).
Worth to practice	Pilot study, does not demonstrate any advantage for infusing small amounts of lidocaine into the endometrial cavity to reduce pain associated with IUD insertion.
Level of evidence	I (pilot study)
Notes	Provides data on mean pain scores and percentage of women experiencing moderate to severe pain with IUD insertion (pain ≥ 3).

Citation	Ngo, L. L., Ward, K. K., & Mody, S. K. (2015). Ketorolac for pain control with intrauterine device placement. *Obstetrics and gynecology*, *126*(1), 29-36.
Design/Method	Randomized, double-blind, placebo-controlled trial. University of California San Diego Women's Health Clinics.
Population	67 nulliparous or multiparous women aged 18 to 51 years.
Variables/Intervention	Ketorolac 30 mg or placebo of normal saline injected into upper outer quadrant of gluteus muscle 30 min prior to insertion.
Measurement	Pain level on a visual analog scale from 0 cm (no pain) to 10 cm (worst pain possible). Questionaire at 15-minute post procedure to assess possible side effects from study drug. Providers completed questionnaire including level of training, type of IUD, purpose, uterine position, and any complications.
Data analysis	57 participants needed to obtain 80% power with a 5% α error rate. Power calculation based on previous studies using 10-cm VAS. Data analyzed based on an intention-to-treat analysis. Pain scores (continuous variables) compared using Wilcoxon rank-sum test as had a nonnormal distribution. The χ^2 for categorical variables and *t* test or Wilcoxon rank-sum test for continuous variables. PASW Statistics 18 and SAS 9.4 software.
Findings	No difference in median pain scores during IUD placement between the placebo compared with ketorolac groups (5.2 compared with 3.6 cm, $p = .99$). Decrease in median pain scores after IUD insertion at 5 minutes (2.2 compared with 0.3 cm, $p \leq .001$) and 15 minutes (1.6 compared with 0.1 cm, $p \leq .001$). Nulliparous women (n = 16) had a decrease in pain scores with IUD placement (8.1 compared with 5.4 cm, $p = .02$). Post procedure health questionnaire revealed significantly more participants in placebo group received acetaminophen at 15 minutes after IUD insertion compared with the ketorolac group (52% compared with 21%, $p = .02$).
Worth to practice	Ketorolac does not reduce pain with IUD insertion but does reduce pain at 5 and 15 minutes after placement. Study does support intramuscular ketorolac for decreasing pain after IUD insertion. Study not powered to detect a difference less than 2.0 cm. Nulliparous participants showed a decrease in pain, but this study was not powered for subgroup analysis for parity, and small sample size of 16 nullips – may be result of chance and may not be generalizable. Ketorolac relatively inexpensive (approximately $1 per dose), can be stocked in clinics, wait time of 30 mins compared with 1 h for oral NSAIDs, analgesia lasting 4 – 6 h. Need for potentially painful IM injection and in-clinic wait time of 30 mins. Health care provider must be available to administer the injection.
Level of evidence	I
Notes	Clinically significant difference in VAS defined as 1.3 – 2.0 cm, researchers used a difference of 2.0 cm. Questionaire revealed few minor side effects from study drug. Majority of participants felt pain

	form injection was “not as bad” as pain from IUD placement (71% compared with 81%); however, participants (22% in placebo group and 18% in ketorolac group) reported injection pain was as painful as IUD placement. Median pain scores higher in nulliparous subgroup compared with multiparous subgroup (8.1 compared with 3.7 in placebo arm and 5.4 compared with 2.5 cm in ketorolac arm). Maximal effect of ketorolac at 1 – 2 h, but study done at time of onset, 30 mins.

Citation	Scavuzzi, A., Souza, A. S., Costa, A. A., & Amorim, M. M. (2013). Misoprostol prior to inserting an intrauterine device in nulligravidas: A randomized clinical trial. *Human Reproduction, 28*(8), 2118-2125.
Design/Method	Randomized, double-blinded clinical trial.
Population	179 nulligravid of reproductive age.
Variables/Intervention	Misoprostol 400 mcg or placebo into posterior vaginal fornix by investigator 4 h prior to IUD insertion.
Measurement	Women judged pain subjectively using VAS 0 = absence of pain, 10 = worst pain imaginable, later dichotomized into absent/mild (0 - 5) and moderate/severe (6 - 10). Subjective difficulty as reported by the investigator.
Data analysis	Sample size of 152 deemed necessary using OpenEpi software program. Distribution tables of frequency for categorical variables, and measures of central tendency and dispersion calculated for numerical variables. Fisher's exact test and χ^2 test of association and two=tailed values for all tests. Risk ratios (RR) calculated as a measure of relative risk with relevant 95% confidence intervals (CI). Number needed to treat (NNT) and number needed to harm (NNH) calculated with respective 95% CI.
Findings	The misoprostol group had a 44% reduction in moderate-to-severe pain compared with the placebo group (RR = 0.56; 95% CI: 0.41 - 0.76; NNT = 3; P = 0.00004). Significant differences were found with less difficulty in inserting the IUD (RR = 0.49; 95% CI: 0.33 = 0.72; NNT = 3; P = 0.00001). No significant differences in frequency of side effects such as nausea, vomitinf, hyperthermia, and diarrhea, but there was a significant increase in cramps in the misoprostol group compared with placebo (RR = 1.40; 95% CI: 1.05 - 1.86; NNH = 6; P = 0.002).
Worth to practice	Use of misoprostol 400 mcg vaginally inserted by the provider four hours pre-insertion of IUD was found to be associated with less subjective difficulty in inserting the IUD in nulligravidas, and less pain as reported by the women; however, there was a greater incidence of cramps. The effect of misoprostol on the cervix makes its use a feasible proposition for certain gynecological procedure, but may not be feasible / may be detrimental to overall choice of this method due to 4 h interval between dosing and insertion. Use it in group of women provider deems necessary to reduce pain and facilitate insertion ease. NNT to evaluate actual benefits in clinical practice: for every three IUD insertions, with prior use of misoprostol, one woman would have an easier procedure.
Level of evidence	1
Notes	Principal investigator inserted all interventions and IUDs. Good discussion of how misoprostol could work and rationale for using vaginally vs orally at time interval of 4 h.

Citation	Singh, R., Thaxton, L., Carr, S., Leeman, L., Schneider, E., & Esprey, E. (2015). Nitrous oxide for intrauterine device insertion in nulliparous women: A randomized controlled trial.
Design/Method	Double blind, randomized controlled trial
Population	80 nulliparous women, aged 13 - 45 years
Variables/Intervention	50/50 nitrous oxide with oxygen or oxygen alone through a mask
Measurement	100-mm visual analog scale for pain. Satisfaction with pain management on a 5-point Likert scale
Data analysis	Sample of 80 women needed to determine a clinically significant difference in mean VAS scores of 15 mm with 80% power and $\alpha = 0.05$. Mean scores.
Findings	Mean maximal pain scores were similar between groups (54±25mm[nitrous oxide] compared with 55±21 [oxygen]; p =.85). Women in nitrous group were more satisfied with their pain management (67.5% vs 42.5%; p = .04) on the Likert scale.
Worth to practice	No adverse effects. Women expressed satisfaction even though it did not reduce their pain (anxiolytic). Sets in rapidly, inexpensive, noninvasive, easily reversible.
Level of evidence	I
Notes	Nitrous works in so many pathways. Has analgesic and amnesic effects.

Citation	Swenson, C., Turok, D. K., Ward, K., Jacobson, J. C., & Dermish, A. (2012). Self-administered misoprostol or placebo before intrauterine device insertion in nulliparous women. *Obstetrics & Gynecology*, *120*, 341-347.
Design/Method	Randomized controlled trial. Outpatient obstetrics and gynecology clinic, University of Utah.
Population	105 nulliparous age 18 years or older.
Variables/Intervention	Misoprostol 400 mcg or placebo vaginally or bucally 3 - 4 hours before insertion.
Measurement	Pain rated by participants using validated 100-mm visual analog scale (0 = none, 100 mm = worst imaginable). Healthcare provider addressed ease of insertion based on visual analog scale (0 = extremely easy, 100 mm = impossible).
Data analysis	Sample size and power calculation determined to detect a 15-mm difference in participant perceived pain. For $\alpha = 0.05$ and 90 % power, 50 participants needed in each group. Wilcoxon Mann-Whitney used because variables of interest failed to meet Shapiro-Wilks normality assumption. STATA version 10.0 software.
Findings	94% chose to insert vaginally (n = 99), data was analyzed excluding buccal administration (n = 6). No significant difference in pain during IUD insertion. ($p = .74$). Pain significantly higher before IUD insertion in misoprostol group (mean 17.1 mm) versus the placebo group (mean 4.7 mm); $p = .003$). Healthcare provider ease of insertion was not significantly different between the two groups (misoprostol mean 25 mm, placebo mean 27.4 mm, $p = .64$).
Worth to practice	Self-administered misoprostol 3 - 4 hours before IUD insertion in nulliparous women does not reduce patient-perceived pain, and does not increase healthcare provider ease of insertion.
Level of evidence	1
Notes	Healthcare providers having placed 10 or more IUDs in past year.

Citation	Tavakolian, S., Doulabi, M. A., Baghban, A. A., Mortazavi, A., & Ghorbani, M. (2015). Lidocaine-Prilocaine cream as analgesia for IUD insertion: A prospective, randomized, controlled, triple-blinded study. *Global Journal of Health Science*, *7*(4), 399-404.
Design/Method	Prospective, randomized, controlled, triple-blinded study.
Population	92 women, multiparous
Variables/Intervention	EMLA cream containing 25 mg lidocaine and 25 mg prilocaine or placebo cream applied to cervix using cotton swab, 7 minutes prior to IUD insertion.
Measurement	Visual analog score 10-cm where 0 means no pain and 10 the most severe pain. Tated as 0 for no pain, 1-3 for mild pain, 4-6 for average pain, 7-9 for severe pain and 10 for worst pain ever.
Data analysis	Descriptive and inferential statistics. Chi square and Fisher's exact test for demographic and confounding variables. Quantitative variables compared using independent t test or Mann-Whitney test. Significant if $p < 0.05$. SPSS 17
Findings	Significant difference in pain between the two groups 4.61±2.55 in the placebo group and 2.65±2.53 in the EMLA group; $p < 0.001$.
Worth to practice	Topical EMLA cream reduces pain during IUD insertion but seven minutes was allocated for the anesthetic to work.
Level of evidence	I
Notes	Discusses differences in pain transmission in uterus versus cervix.

Citation	Tornblom-Paulander, S., Tingaker, B. K., Werner, A., Liliecreutz, C., Conner, P., Wessel, H., & Ekman-Ordeberg, G. (2015). Novel topical formulation of lidocaine provides significant pain relief for intrauterine device insertion: A pharmacokinetic evaluation and randomized placebo-controlled trial. *Contraception*, *103*(2), 422-427.
Design/Method	Phase-I : single-arm pharmacokinetic study. Phase-II: randomized, double-blind, placebo-controlled trial studies. Karolinska University Hospital, Stockholm, and three public hospitals, Sweden.
Population	Women aged older than 18 years, no restrictions on previous childbirth.
Variables/Intervention	Phase-I: Single 8.5-mL dose of lidocaine gel (1 mL onto portio surface, 2 mL into cervical canal, and 5.5 mL into uterine cavity) 5 minutes before IUD insertion. Phase-II: Lidocaine or a placebo gel with IUD insertion taking place within 5 mins.
Measurement	Phase-I: Blood samples at baseline, and at 5,10,20,30,60,120, and 180 mins after lidocaine administration. Pain assessed on a 100-mm VAS. Phase-II: Patient rated maximum pain level on 100-mm VAS.
Data analysis	Phase-I: Sample size of 15 to determine pharmacokinetic parameters: maximum plasma concentration (C_{max}), time taken to reach maximum concentration (t_{max}). Results presented as mean ± SD or absolute values. Phase-II: Sample size of 172 would provide statistical significance at the 5% level, and 90% power. Comparison performed using analysis of variance (ANOVA), expressed as mean difference with 95% confidence level. Stratified ANOVA to investigate relationships between VAS pain and IUD type, midwife, volume of lidocaine administered, and degree of discomfort.
Findings	Phase-I: Pharmacokinetic parameters were C_{max} 351 ± 205 ng/mL, and t_{max} 68 ± 41 minutes). Considerable individual variation in absolute plasma levels; highest value for C_{max} 725 ng/mL and lowest value was 64.7 ng/mL. Pain scores on VAS were low, with mean values < 9 mm. Association between C_{max} and pain relief observed, with almost complete pain relief in 6 of 7 women with C_{max} > 350 ng/mL. No serious adverse events. Phase-II: Mean VAS score for maximum pain significantly lower in the lidocaine group than in the placebo group (28.3 vs. 44.2; $p < 0.001$). Mean between-group difference was 15.0 representing a 36% reduction in VAS score in the lidocaine group. Significantly higher percentage in lidocaine group considered to be essentially pain-free (VAS score ≤10 mm), and significantly lower percentage had moderate to severe pain (VAS score > 40 mm). Stratified ANOVA showed neither discomfort during administration of the study treatment nor IUD type influenced the effect of lidocaine.
Worth to practice	Study shows administration of lidocaine, as a short-acting 4% viscous solution, 5 minutes before insertion of an IUD provides pain relief. Benefits of lidocaine evident in several ways: significantly reduced

	mean VAS score; high percentage reduction in mean VAS score; higher percentage of women with lower maximum pain; significantly higher percentage of women who were essentially pain-free; and a significantly lower percentage of women with moderate to severe pain. Duration of pain relief with lidocaine between 30 and 60 minutes.
Level of evidence	I
Notes	Percentage of women reporting no or a little discomfort during administration of study drug was greater in the lidocaine group (63.6%) than in the placebo group (47.2%) representing a statistically significant difference (p = .023).